

FLUORIDATION AND CANCER

THE BIOLOGY AND EPIDEMIOLOGY OF BONE AND ORAL CANCER RELATED TO FLUORIDATION

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SUMMARY: Recent studies showing substantial increases in the incidence of bone cancer and osteosarcoma in males (but not females) exposed to fluoride gave us the unique opportunity of using females as a control group to determine whether there is a link between fluoridation and bone cancer in males. Using three different data bases, we found that 1) the bone cancer incidence rate was as much as 0.95 cases a year per 100,000 population higher in males under age 20 living in fluoridated areas; 2) the osteosarcoma incidence rate was 0.85 new cases a year per 100,000 population higher in males under age 20 living in fluoridated areas; and 3) for males of all ages, the bone cancer death rate and bone cancer incidence rate was as much as 0.23 and 0.44 cases higher per 100,000 population, respectively, in fluoridated areas. These findings indicate that fluoridation is linked to an increase in bone cancer and deaths from bone cancer in human populations among males under age 20 and that this increase in bone cancer is probably all due to an increase in osteosarcoma caused by fluoride. Results indicating a fluoridation-linked 30-60% increase in oral cancers are also presented.

Key words: Bone; Cancer; Fluoridation; Fluoride; Mortality; Mouth; Oral; Osteosarcoma.

Introduction

Numerous studies have shown that fluoride causes genetic damage (1-28), at levels as low as one-half part per million (0.5 ppm) in cell cultures (1) and at exposures as low as 1 ppm in the drinking water (18). It is generally agreed that substances which cause genetic damage are also likely to cause cancer. Since the level of fluoride used to fluoridate public drinking water is 0.7-1.2 ppm, individuals living in fluoridated areas may suffer an increased risk of genetic damage and cancer.

Early studies indicated that fluoride can induce abnormal cell proliferation and transformations. In the first study ever done examining the effect of fluoride on animals, a thickening in the neck region was observed (29). Fluoride was later reported to induce cell proliferation in the thyroid (30) and possibly in the lymph glands (31). Exostoses (or what some consider to be tumorous bony outgrowths) of the carpal joint (32), metatarsal bone (33), tibia (34), maxilla (35), mandible (36) and femur (37) have also been observed. Fluoride was found to increase the number of myelocytes (38) and normoblasts (39) (red blood cells with pycnotic nuclei) in the blood. Odontoblasts with pycnotic nuclei were reported (40). Fluoride-induced abnormalities in ameloblasts included the appearance of squamous cells (36) and the appearance of abnormal nuclei (41).

More recently researchers have shown that increasing levels of fluoride increased the incidence of melanotic tumors in fruit flies (42). In patients receiving fluoride to treat their osteoporosis, fluoride was shown to transform white blood cells into cells

"suggestive of reticuloendothelial malignancy" (43). Others have since found that fluoride transforms normal cells into cancer cells (27,44-45), and that it promotes and enhances the carcinogenicity of other cancer-causing chemicals (44).

From 1975 to 1977, we conducted epidemiological studies showing that 10,000 or more cancer deaths per year were linked to water fluoridation in the US (46-49). Although this research was contested by others (50-52), corrections of their studies for omissions and mathematical errors confirmed a fluoridation-linked increase in cancer death rate (53-55). Other studies, though not as large, also indicated a possible fluoridation-cancer link (56-58). This heated debate led to US Congressional subcommittee hearings on the issue in 1977 and at the conclusion of these hearings the chairman, Representative L H Fountain, stated: "... at the present time the carcinogenicity, or lack of carcinogenicity, of this substance is a question which remains unanswered" (59) and his subcommittee instructed the US Public Health Service to conduct an investigation to determine whether or not fluoride causes cancer in animals.

In 1989, the results of this study were released. The principal finding was the fluoride-linked occurrence of a rare form of liver cancer (hepatocholangiocarcinoma) in both male and female mice (60). This study also showed that as dietary fluoride increased, so did the incidence of squamous cell metaplasias (precarcinogenous cell changes) and tumorous or cancerous squamous cells in the mouths of both male and female rats. In male (but not female) rats exposed to fluoride, this study found a rare form of bone cancer (osteosarcoma) (61).

Studies by Procter and Gamble scientists showed that the incidence of pre-cancerous growths in oral tissues increased as exposure to fluoride increased (62). They also concluded: "There is clearly a compound[fluoride]-related increase in osteomas in both male and female mice (63)." In addition, they tabulated bone cancers and tumors in rats fed fluoride, but not in untreated rats (64).

The National Cancer Institute and the New Jersey Department of Health published independent studies showing substantial increases in the incidence of osteosarcoma in males, but not females, under the age of 20 residing in fluoridated areas (65,66). Others have claimed they were unable to find such a link (67-70).

The present study presents data on bone and oral cancer. Figures for the incidence of hepatocholangiocarcinoma are not available. The fact that both animal studies and human studies indicate a fluoride-linked bone cancer increase in males only allows us to do a very definitive epidemiological study. We can use females to serve as an excellent control group for males residing in the same localities. By subtracting the bone cancer rate of females from that of males, we can eliminate the effect of factors that increase or decrease bone cancer in both males and females and confine our study only to factors that affect bone cancer in males.

Methods

Bone cancer and osteosarcoma incidence rates for white males and females were obtained and derived from the Surveillance, Epidemiology and End Results (SEER) program of the National Cancer Institute (NCI) through one of their publications (65) and from the New Jersey Department of Health (66). To examine deaths from bone cancer in relation to fluoridation in 26 areas we had previously studied with regard to cancer mortality (71), bone cancer death rates for white males and females were obtained from "Cancer Mortality by County: 1950 to 1969" (72).

Female rates were subtracted from male rates to yield "net bone cancer incidence (or death) rates". These rates are given in terms of excess cases (or deaths) in males per 100,000 population per year.

Results

I. The incidence of bone cancer and fluoridation.

Cancer incidence data for 1973-1987 were collected by the National Cancer Institute from the SEER program, a network of 9 centers around the USA which continually measure the cancer incidence of approximately 10% of the US population. From these areas, investigators at the NCI selected white residents of counties which fulfilled their criteria for being put into one of two groups: fluoridated (F) and non-fluoridated (NF) (65,73). They reported age-adjusted bone cancer incidence data for all whites and male whites from each of these two groups for two time periods: 1973-1980 and 1981-1987. From these data, we calculated the bone cancer incidence rates of white females. Subtracting the female bone cancer incidence rates from the male bone cancer incidence rates yielded "net bone cancer incidence rates", male minus female. By averaging cancer rates from 1973-1980 and 1981-1987, cancer rates for "1973-1987" were calculated. From Table 1, it can be seen that there are 0.31 (or 0.44 among those exposed the longest) additional cases of bone cancer among males per 100,000 population per year in fluoridated areas. This amounts to about a 50% higher bone cancer rate for males living in fluoridated areas.

TABLE 1. Net bone cancer incidence rates (male rates minus female rates) in fluoridated (F) and nonfluoridated (NF) populations in SEER areas (65)*

	Net Bone Cancer Rate per 100,000 Population per Year		
	1973-1980	1981-1987	1973-1987
F	0.34	0.40	0.37
NF	0.16	-0.04	0.06
Difference			
F - NF	0.19	0.44	0.31

* Age adjusted US 1970

The data necessary to calculate the figures in Table 1 were also given for various age groups. Since primary interest concerns the effect of fluoridation on males under age 20 (65,66), values comparable to those reported in Table 1 were calculated for males in this age group (Table 2).

TABLE 2. Net bone cancer incidence rates (male rates minus female rates) in fluoridated (F) and nonfluoridated (NF) populations aged 0-19 years in SEER areas (65)*

	Net Bone Cancer Rate per 100,000 Population per Year		
	1973-1980	1981-1987	1973-1987
F	0.31	0.56	0.44
NF	-0.29	-0.39	-0.34
Difference			
F - NF	0.59	0.95	0.77

* Age adjusted US 1970

From Table 2, it can be seen that there are 0.77 (or 0.95 among those exposed the longest) additional cases of bone cancer among males under age 20 per 100,000 population per year in fluoridated areas. This amounts to over a 100% higher bone cancer rate among males under age 20 living in fluoridated areas.

Age-sex-specific osteosarcoma incidence data for 1979-1987 were collected by the New Jersey Department of Health for males and females residing in fluoridated and nonfluoridated municipalities in seven counties in central New Jersey. Subtracting the female osteosarcoma incidence rates from the male osteosarcoma incidence rates yielded "net osteosarcoma incidence rates", male minus female. From Table 3, it can be seen that there are 0.85 additional cases of *osteosarcoma* among males under age 20 per 100,000 population per year in fluoridated areas. This compares to an increase in *bone cancer* incidence of 0.95 for those exposed to fluoridation the longest (Table 2).

TABLE 3. Osteosarcoma incidence rates (1979-1987) in fluoridated (F) and nonfluoridated (NF) populations aged 0-19 years in New Jersey (66)*

	Osteosarcoma Rate per 100,000 Population per Year		
	Males	Females	(Male minus Female)
F	1.20	0.31	0.89
NF	0.35	0.31	0.04
Difference			
F - NF	0.85	0.00	0.85

* Not age adjusted

II. Death rate from bone cancer and fluoridation

Average age-adjusted cancer death rates of white males and white females (all ages) for the period from 1950 to 1969 were obtained from "Cancer Mortality by County: 1950 to 1969" (72) for a group of 26 areas previously studied by us (71). Five of these areas are fluoridated cities in counties that are 100% fluoridated (F); five of these areas are fluoridated cities in counties that contained some nonfluoridated areas (F*); thirteen of these areas are cities that were not fluoridated as of 1969 (NF); and three areas are cities that were fluoridated after 1964 but before 1969 (BF). County data from each of those areas were obtained. In each, the female bone cancer death rate was subtracted from the male bone cancer death rate to yield 26 individual "net bone cancer death rates", male minus female. These values are listed in Table 4.

The data from Table 4 were averaged for various groupings of fluoridated and nonfluoridated areas, and these values are compared in Table 5. The average "net bone cancer death rate" is higher in the fluoridated areas than in nonfluoridated areas in each of the 5 comparisons made, and in each of the comparisons the difference is statistically significant (a "t" value of >1.75 indicates significance at the P<.05 level). For example, a comparison of those areas that are 100% fluoridated (F) with those areas where most of the area was never fluoridated (NF) yields a fluoridation-linked increase in "net bone cancer death rate" of 0.23 per 100,000 population.

The data from Table 1 for males of all ages show an increase of 0.31 *new cases* of bone cancer per 100,000 population per year in fluoridated areas. This is consistent with the value of about 0.20 bone cancer *deaths* per 100,000 per year obtained in Table 5.

Comparing the values in Table 2 of 0.77-0.95 additional cases of *bone cancer* and the Table 3 value of 0.85 additional cases of *osteosarcoma* among males under age 20 per 100,000 population per year in fluoridated areas strongly suggests that the fluoridation-linked increase in bone cancer is totally due to an increase in osteosarcoma caused by fluoride.

TABLE 4. Net bone cancer death rates (male rates minus female rates) in completely fluoridated (F), primarily fluoridated (F*), barely fluoridated (BF), and nonfluoridated (NF) populations (1950 to 1969) (72)**

Net Bone Cancer Death Rate per 100,000 Population per Year (Male Rate Minus Female Rate)		
F	St. Louis	0.9
F	Philadelphia	0.7
F	San Francisco	0.7
F	Baltimore	0.7
F	Washington DC	0.4
F*	Pittsburgh	0.8
F*	Cleveland	0.7
F*	Buffalo	0.5
F*	Chicago	0.5
F*	Milwaukee	0.4
BF	Detroit	0.8
BF	New York City	0.5
BF	Dallas	0.5
NF	Boston	0.8
NF	Newark	0.7
NF	Kansas City	0.7
NF	Portland	0.5
NF	Columbus	0.5
NF	Cincinnati	0.5
NF	Atlanta	0.4
NF	Los Angeles	0.3
NF	Seattle	0.3
NF	New Orleans	0.3
NF	San Antonio	0.3
NF	San Diego	0.3
NF	Houston	0.2

** Age adjusted US 1960

TABLE 5. Differences in net bone cancer death rates (male rates minus female rates) in various groupings of fluoridated and nonfluoridated areas of Table 4

Fluoridated Group	Nonfluoridated Group	Net increase in fluoridated group	"t" values
F	NF	0.23	2.242
F	NF + BF	0.21	2.018
F + F*	NF	0.18	2.300
F + F*	NF + BF	0.16	2.012
F + F* + BF	NF	0.18	2.443

III. The incidence of oral cancer and fluoridation.

The NCI also reported cancers of the oral cavity and pharynx (73) for whites. The figures in Table 6 are derived from those data.

TABLE 6. Ratios of oral cancer in fluoridated areas/oral cancer in nonfluoridated counties in the Iowa and Seattle SEER areas (73) and both areas combined for the 1973-1987 survey period

Years of exposure	Iowa F/NF	Iowa cases	Seattle F/NF	Seattle cases	Iowa + Seattle F/NF
0-4	1.20	31	1.00	81	1.06
5-9	1.40	38	1.20	500	1.21
10-14	1.70	116	1.20	577	1.28
15-19	1.60	210	0.80	292	1.13
20+	1.60	848	-	-	1.60
All periods	1.59	1243	1.11	1450	1.33

From Table 6 it can be seen that as exposure to fluoridation increased, so did the incidence of oral cancer. These data, which show a 30-50% increase in the cancer incidence rate of the oral cavity and pharynx in fluoridated areas, are far more serious than the bone cancer data. Nationally, they translate into 6000-9000 additional cases of oral and pharyngeal cancer per year in the USA as a result of fluoridation. Additionally, the laboratory data supporting fluoride-induced oral tumors and cancers are far more convincing than the data on bone cancer (61).

Discussion

Four studies have been published claiming that fluoride does not cause bone cancer and/or osteosarcoma. There are major deficiencies in these studies.

1. A study by Hrudey and coworkers used a population in Alberta, Canada, far too small to give meaningful results (67). By their own admission, "these data do not allow any definitive conclusions about the role of fluoridation as a risk factor for osteosarcoma in humans ... with so rare a tumor in populations the size of Calgary and Edmonton, stable rates and statistical significance are never likely to be achieved."
2. Based on 1 or 2 osteosarcoma patients of unspecified age and sex who spent more than one-third of their life or childhood in an area whose drinking water contained more than 0.7 ppm fluoride and 6 or 7 osteosarcoma patients of unspecified age and sex who spent less than one-third of their life or childhood in an area whose drinking water contained more than 0.7 ppm fluoride, McGuire and coworkers (69) suggest that "fluoridation at recommended levels may provide a protective effect against the formation of osteosarcoma." This study did not examine bone cancer incidence rates, nor present data upon which a conclusion regarding the effect of fluoride exposure on osteosarcoma could be made. Provisions to assure a significant and meaningful difference in fluoride exposures of what were termed "high" and "low" were not made.
3. Mahoney and coworkers admit that there has been an increase in bone cancer among males under 30 years of age since fluoridation was instituted in New York

State, but they claim that there was no apparent difference in bone cancer incidence rates in fluoridated and non-fluoridated areas (68). From Table 7, it can be seen that by calculating net bone cancer incidence rates (male rates minus female rates), there are 0.37 additional cases of bone cancer among males under 30 years of age per 100,000 population per year in the fluoridated areas.

TABLE 7. Net bone cancer incidence rates (male rates minus female rates) in fluoridated (F) and nonfluoridated (NF) populations aged 0-29 years in New York State (68)*

Net Bone Cancer Rate per 100,000 Population	
F	0.67**
NF	0.30
Difference (F - NF)	0.37

* Not age adjusted

** Since the nonfluoridated areas are about 93% nonSMSA and 7% SMSA, this same proportion was taken to determine the cancer rates and thus the net cancer rate for the fluoridated areas (SMSA = Standard Metropolitan Statistical Area).

4. The data from the study of Freni and Gaylor (70) are not as reliable as the NCI (65) and the New Jersey (66) data because, while Freni and Gaylor identify cities and states that are fluoridated and nonfluoridated, the cancer registry areas covered by these cities and states are much larger and sometimes include both fluoridated and nonfluoridated locations, e.g. Seattle and Iowa. Nonetheless, by calculating net bone cancer incidence rates (male rates minus female rates) from their data, what appeared to be fluoridation-linked increases in bone cancer incidence rates were observed (Table 8). It is difficult to understand how these investigators could have come to any conclusions, since they mistabulated or had no knowledge of the fluoridation status of 20 of the 35 areas in their study.

TABLE 8. Net bone cancer incidence rates (male rates minus female rates) in fluoridated (F) and nonfluoridated (NF) populations (mostly for the period 1983-1987) (70)*

	Net Bone Cancer Rate per 100,000 Population per Year				
	US [□]	Canada [†]	UK [‡]	Europe [§]	Australia/New Zealand [§]
F	0.36	0.44	0.30	-	0.20
NF	0.05	-0.10	0.27	0.07	-
Difference (F - NF)	0.31	0.54	0.03		

* Age adjusted world.

[□] NF consists of Los Angeles and Utah; F consists of San Francisco, Connecticut, Atlanta, Iowa, Detroit, New Mexico, New York City, New York Upstate, Puerto Rico, Seattle, New Orleans.

[†] NF consists of British Columbia which is 10% fluoridated; F consists of the rest of Canada which is 40-70% fluoridated (74).

[‡] F consists of Birmingham which is fluoridated; NF consists of Northwest, Oxford, South Thames, Southwest, Trent, Mersey, and Scotland which are not fluoridated (75), but the estimated fluoride consumption from tea is approximately 1-2 mg per day.

[§] NF consists of Denmark, Norway and Sweden which are not fluoridated; East Germany which is 20% fluoridated and Finland which has a widely used fluoride tablet program are not included in either group; F consists of Australia which is 66% fluoridated and New Zealand which is 50% fluoridated (76).

Two other investigators, even though they revealed substantial and significant fluoridation-linked increases in bone cancer incidence rates among males 0-19 years of age, tried to either minimize or discount their results.

The New Jersey Health Department, out of concern that fluoridation might be linked to increased rates of osteosarcoma, studied osteosarcoma rates in New Jersey and found male osteosarcoma rates 3-8 times higher in fluoridated areas. It is interesting to note that they changed the title of their report from "A Brief Report on the Association of Drinking Water Fluoridation and the Incidence of Osteosarcoma among Young Males" to "An Epidemiologic Report on Drinking Water and Fluoridation" within a month after its publication.

Although the NCI studies on bone cancer in humans indicated a 30-40% increase in bone and joint cancer incidence rate among males under the age of 20, the authors rationalize away this increase as follows. They reasoned that if an area was fluoridated before 1955, it should show a smaller increase in cancer incidence rate from the 1973-1980 survey to the 1981-1987 survey (since virtually all boys would have had the opportunity for life-long exposure during both periods) than areas fluoridated after 1965, if fluoridation were the cause. Since the cancer incidence rate (from the 1973-1980 survey to the 1981-1987 survey) increased more in the group fluoridated before 1955, the NCI concluded that fluoridation was not responsible for the increase in bone cancer. However, looking at the increase in net cancer incidence rate (male minus female) from the 1973-1980 survey to the 1981-1987 survey, it is found that a greater increase occurs in the group fluoridated after 1965 ($F > 1965$) than in the group fluoridated before 1955 ($F < 1955$). See Table 9, also derived from NCI data (65).

TABLE 9. Net bone cancer incidence rates (male rates minus female rates) in populations aged 0-19 residing in nonfluoridated (NF) areas and in areas fluoridated before 1955 ($F < 1955$) and after 1965 ($F > 1965$) for the two survey periods (1973-1980 and 1981-1987) and the increases in net bone cancer incidence rates from one survey period to the other.*

	Survey Periods		Increase from 1973-1980 to 1981-1980
	1973-1980	1981-1987	
NF	- 0.29	- 0.39	- 0.10
F	0.31	0.56	0.25
$F < 1955$	0.60	0.62	0.01
$F > 1965$	0.29	0.58	0.29

* Age adjusted US 1970

Furthermore, the net bone cancer incidence rates for those populations exposed to fluoridation before 1955 ($F < 1955$) are higher than net bone cancer incidence rates in those exposed after 1965 ($F > 1965$) for the entire survey period (1973-1987), as one would expect. See Table 10, also derived from NCI data (65).

Careful reading also suggests serious shortcomings in how data were treated in the NCI report. At one point, the authors themselves pointed out the pitfalls in another method they used to discount their results. They admitted: "The method of analysis used in this study . . . has some potential disadvantages. Different counties at different time periods were grouped according to their relation to the time of

TABLE 10. Net bone cancer incidence rates (male rates minus female rates) in populations aged 0-19 residing in nonfluoridated (NF) areas and in areas fluoridated before 1955 (F<1955) and after 1965 (F>1965) for the entire survey period (1973-1987).*

	All ages	Ages 0-19
NF	0.06	- 0.34
F<1955	0.61	0.61
F>1965	0.32	0.43

* Age adjusted US 1970

fluoridation ... if a large county or grouping of counties had an unusual cancer experience, and appeared at only one end or other of the time-to-fluoridation grouping, then the patterns ... could be biased" (73). The NCI authors also used this method in an attempt to rationalize away the 30-50% increase they found in cancers of the oral cavity and pharynx.

Newburgh, New York, was one of the first cities in the United States to be fluoridated. In 1956, eleven years after fluoridation was instituted, Caffey, a professor of clinical pediatrics at the College of Physicians and Surgeons, Columbia University, noted cortical defects in the bone X-rays of 13.5% of the children living in fluoridated Newburgh, compared to only 7.5% in the neighbouring nonfluoridated town of Kingston (77). The difference was statistically significant and substantive. Dr Caffey had already noted that these bone defects were strikingly similar to those of osteogenic sarcoma, otherwise known as osteosarcoma (78). In commenting on this observation, the author of the fluoride section of the National Academy of Sciences report "Drinking Water and Health" pointed out: "While progression of cortical effects to malignancies has not been observed clinically, it would be important to have direct evidence that *osteogenic sarcoma rates in males under 30* have not increased with fluoridation" (79).

Since fluoride induces the transformation of fibroblasts into fibrosarcomas (27), one might also expect it to induce the transformation of osteoblasts into osteosarcomas. Biologically, it is reasonable that fluoride, while causing bone cancer in males, might not cause bone cancer in females. Fluoride-linked bone cancer is noticed in males at a period of time in their lives when they are shutting off bone growth by a process (the production of testosterone) that takes longer than the way in which females shut off bone growth (estrogens). By taking advantage of these differences, fluoride could easily induce osteosarcomas in males and not in females. In fact, studies show that 1 ppm fluoride depresses testosterone synthesis *in vitro* (80). Researchers from Battelle and the National Institute of Environmental Health Sciences pointed out: "with the *single* chemical previously studied by the NTP, which induced a clear increase in osteosarcomas in rats, the response was seen in males and not females" (81).

Our data regarding the effect of fluoridation on mortality from all cancers (48) has repeatedly been criticized for supposedly not simultaneously correcting our figures for age, race and sex. While we made these corrections as early as 1976 (49), Table 11 gives the clearest indication of the age-race-sex corrections of our figures. An increase of 10.3 fluoridation-linked cancer deaths per 100,000 population per year over the period 1953-1968 is observed.

TABLE 11. Fluoridation-linked cancer deaths per 100,000 population per year corrected for age, race and sex*

Before initiation of fluoridation	During initiation of fluoridation	After initiation of fluoridation		
1940-1949	1953-1956	1957-1960	1961-1964	1965-1968
0	4.3	7.3	7.8	10.3

* Using US 1950 as reference population

The Knox Report (82) has criticized us for using intercensal years, saying "It would be safer to avoid this source of possible error by adopting the normal practice of centering the calculation of the standardized mortality ratios (SMRs) on, or closely around, the census years, thus using population estimates which would be expected to be more reliable." Using figures taken on and closely around the census years of 1950 and 1970, we found a fluoridation-linked increase of 7.1 cancer deaths per 100,000 per year. Confronted with these figures, Sir Richard Doll admitted that there was an absolute increase in cancer death rate in fluoridated areas (83):

Queen's Counsel. "Well, the figures speak for themselves, don't they, and would you agree that in general terms they show, whichever method you use, that the fluoridated cities do worse than the non-fluoridated cities in comparison as to what happened between 1950 and 1970?"

Doll: "Yes, I do agree, and that is why I said this paper was the first paper which I thought was of any consequence . . ."

Ironically, most of the studies that the Knox report relies upon use intercensal population estimates. In this case, using a pericensal figure around 1970 leads to the inclusion of some cities in the control group that were fluoridated between 1970 and 1972. Nevertheless, extrapolating the figures of 7.1 and 10.3 to the 130,000,000 Americans who are drinking fluoridated water gives a figure of approximately 9,000 to 13,000 fluoridation-linked cancer deaths in the US per year. This is more than can be accounted for by fluoride-induced bone cancer and oral cancer.

In a recent study by Shupe and coworkers (84), a total of 10 male and 190 female cattle were subjected to low, moderate and high fluoride exposures. Only those animals exposed to high fluoride levels exhibited cancers. One exhibited a squamous cell carcinoma and the other exhibited an "undifferentiated" carcinoma. This rate of 2 fluoride-linked cancers per 87 animals is more than enough to be consistent with our figure of 9,000 to 13,000 fluoridated-linked cancer deaths in the US per year. As could be expected with the small number of male animals used, no osteosarcomas were observed in this study.

Conclusions

From the analyses presented in this report, we conclude that

1. The preponderance of evidence shows that fluoridation is causing an increase in bone cancer and deaths from bone cancer in human populations among males under age 20.
2. The increase in bone cancer attributable to fluoridation may all be due to an increase in osteosarcoma caused by fluoride.

3. The preponderance of evidence shows that fluoridation is causing an increase in oral cancer among human populations.
4. Since fluoride has been linked to bone and oral cancers in animals and humans, its biochemistry and its ability to inhibit the DNA repair enzyme system (85), to accelerate tumor growth rate (86), to inhibit the immune system (87), to cause genetic damage in a number of different cell lines (1-28), and to induce melanotic tumors (42), fibrosarcomas (27), hepatocholangiocarcinomas (60), and other tumors and cancers, strongly indicate that fluoride would have a generalized effect on increasing cancers overall.
5. According to our estimates, over 10,000 cancer deaths are caused each year in the United States by fluoridation; this supports the conclusion that fluoridation is causing other types of cancer in humans.

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References

- 1 Aardema MJ, Gibson DP, LeBoeuf RA: Sodium fluoride-induced chromosome aberrations in different stages of the cell cycle: a proposed mechanism. *Mutation Research* 223 191-203 1989.
- 2 Akhundov VY, Aliev AA, Kulgavin AF, Sarina TN. Effect of combined and separate exogenous vitamin administration on the level of chromosomal aberrations induced by sodium fluoride in rats in subacute experiments. *Izvestiya Akademii Nauk Azerbaidzhanskoi SSR, Seriya Biologicheskikh Nauk* (4) 3-5 1981.
- 3 Albanese R. Sodium fluoride and chromosome damage *in vitro* human lymphocyte and *in vivo* micronucleus assays. *Mutagenesis* 2 (6) 497-499 1987.
- 4 Aliev AA, Arshava EA, Askerov IT. Cytogenetic effect of sodium fluoride treatment of *Allium fistulosum* L seeds. *Izvestiya Akademii Nauk Azerbaidzhanskoi SSR, Seriya Biologicheskikh Nauk* (2) 8-10 1982.
- 5 Aliev AA, Babaev DA: Cytogenetic activity of vitamins in bone marrow cells of rat femurs in sodium fluoride-induced mutation conditions. *Tsitologiya Genetika* 15 (6) 19-23 1981.
- 6 Aliev AA, Kulgavin AE, Sarina TN. Effect of tocopherol on sodium fluoride-induced chromosome aberrations in rat femoral bone marrow cells. *Izvestiya Akademii Nauk Azerbaidzhanskoi SSR, Seriya Biologicheskikh Nauk* (1) 17-20 1981.
- 7 Bale SS, Hart GH. Studies on the cytogenetic and genetic effects of fluoride on barley. I. A comparative study of the effects of sodium fluoride and hydrofluoric acid on seedling root tips. *Canadian Journal of Genetics and Cytology* 15 695-702 1973.
- 8 Bale SS, Hart GH. Studies on the cytogenetic and genetic effects of fluoride on barley. II. The effects of treatments of seedling coleoptiles with sodium fluoride. *Canadian Journal of Genetics and Cytology* 15 703-712 1973.
- 9 Caspary WJ, Myhr B, Bowers L *et al.* Mutagenic activity of fluorides in mouse lymphoma cells. *Mutation Research* 187 165-180 1987.
- 10 Cole J, Muriel WJ, Bridges BA. The mutagenicity of sodium fluoride to L5178Y [wild type and TK +/- (3.7.2c)] mouse lymphoma cells. *Mutagenesis* 1 (2) 156-67 1986.
- 11 He W, Liu A, Bao H *et al.* Effect of fluoride and fluoroacetamide on sister chromatid exchanges and chromosomal aberrations in cultured red Muntjac (*Muntiacus muntjac*) cells. *Huangjing Kexue Xuebao* 3 94-100 1983.
- 12 Jachimczak D, Bogumila S. The effect of fluoride and lead ions on the chromosomes of human leucocytes *in vitro*. *Genetica Polonica* 19 (3) 353-357 1978.
- 13 Jagiello G, Lin J. Sodium fluoride as potential mutagen in mammalian eggs. *Archives of Environmental Health* 29 230-235 1974.
- 14 Kanematsu N. Genetic toxicity of biomaterial. DNA damaging effects of fluoride and other fluorine compounds. *Japanese Journal of Oral Biology* 27 372-4 1985.

- 15 Kishi K, Tonomura A. Mutagenicity of sodium fluoride - review and human lymphocyte assay. *Husso Kenkyu* 5 35-41 1984.
- 16 Mitchell B, Gerdes RA: Mutagenic effects of sodium and stannous fluoride upon *Drosophila melanogaster*. *Fluoride* 6 113-117 1973.
- 17 Mohamed AH, Applegate HG, Smith JD. Cytological reactions induced by sodium fluoride in *Allium cepa* root tip chromosomes. *Canadian Journal of Genetics and Cytology* 8 242-244 1966.
- 18 Mohamed AH, Chandler ME. Cytological effects of sodium fluoride in mice. *Fluoride* 15 (3) 110-118 1982.
- 19 Mohamed AH. Chromosome changes in maize induced by fluorine gas. *Canadian Journal of Genetics and Cytology* 12 614-620 1970.
- 20 Mohamed AH. Cytogenetic effects of hydrogen fluoride gas on maize. *Fluoride* 10 157-164 1977.
- 21 Pati PC, Bhunya SP. Genotoxic effect of an environmental pollutant. *Caryologia* 40 (1-2) 79-87 1987.
- 22 Ragimova GK, Kulgavin AE, Alekperov UK. Features of the modifying capacity of mutations in *Aegilops* seeds produced under various ecological conditions. *Izvestiya Akademi Nauk Azerbaidzhanskoi SSR, Seriya Biologicheskikh Nauk* (4) 21-24 1983.
- 23 Scott D, Roberts SA. Extrapolation from *in vitro* tests to human risks: experience with sodium fluoride clastogenicity. *Mutation Research* 189 (1) 47-58 1987.
- 24 Suzuki N, Tsutsui T. 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. *Shigaku* 77 (2) 436-447 1989.
- 25 Tazhibaev S, Kozahkmetova E, Aldabergenova K, Mamyrbayev A. Modifying effect of nutrition on the mutagenic activity of phosphorus and fluorine compounds. *Voprosy Pitaniya* (4) 63-6 1987.
- 26 Tsutsui T, Suzuki N, Ohmori M, Maizumi H. Cytotoxicity, chromosome aberrations and unscheduled DNA synthesis in cultured human diploid fibroblasts induced by sodium fluoride. *Mutation Research* 139 193-198 1984.
- 27 Tsutsui T, Suzuki N, Ohmori M. Sodium fluoride-induced morphological and neoplastic transformation, chromosome aberrations, sister chromatid exchanges and unscheduled DNA synthesis in cultured Syrian hamster embryo cells. *Cancer Research* 44 938-941 1984.
- 28 Voroshilin S, Plotko E, Gatiyattullina K, Giliova E. Cytogenetic effect of inorganic fluorine compounds on human and animal cells *in vivo* and *in vitro*. *Genetika* 9 (4) 115-120 1973.
- 29 Maumene E. Tests to determine the action of fluorides on the animal organism. *Comptes Rendus, Academie de Sciences* 39 538-450 1854.
- 30 Goldemberg I. Experimental goiter produced by fluorine. *Semana Medica* 28 628-632 1921.
- 31 Pitotti G. On the effects of sodium fluoride on various animal organs and tissues. *Bollettino delle Scienze Mediche Bologna* 4 (7) 5-22 1893. Be
- 32 Rost E. *Berichte* 14, *Internationaler Kongress Hygiene Demographie. Berlin* 4 166 1907.
- 33 Reed OE, Huffman CF. The results of a five-year mineral feeding investigation with dairy cattle. *Michigan State College Experimental Station, Technical Bulletin* 105 363 1930.
- 34 Cristiani H. Appearance of bone lesions in experimental fluorine poisoning. *Comptes Rendus des Seances, Societe de Biologie* 110 416-418 1932.
- 35 Velu H. Darmous, spontaneous fluorosis in phosphate zones. *Archives, Institut Pasteur d'Algerie* 10 41-118 1932.
- 36 Bethke RM, Kick CH, Hill TJ, Chase SW. Effects of diet containing fluorine on jaws and teeth of swine and rats. *Journal of Dental Research* 13 473-493 1933.
- 37 Kick CH, Bethke RM, Edgington BH. Effect of fluorine on the nutrition of swine and special reference to bone and tooth composition. *Journal of Agricultural Research* 46 1023-1037 1933.
- 38 Schwyzer F. The pathology of chronic fluoride poisoning. *Journal of Medical Research* 10 (5) 301-311 1903.
- 39 Leake CD, Ritchie G. The blood picture in dogs following experimental atropic gastritis induced by sodium fluoride. *American Journal of Physiology* 76 234 1926.
- 40 Sutro CJ. Changes in the teeth and bone in chronic fluorine poisoning. *Archives of Pathology* 19 159-173 1935.
- 41 Chaneles J. Estudios sobre el fluor y fluorosis experimental. *Revista Odontologica* (Buenos Aires) 187-224 1930.

- 42 Herskowitz I, Norton I. Increased incidence of melanotic tumors in two strains of *Drosophila melanogaster* following treatment with sodium fluoride. *Genetics* 48 307-310 1963.
- 43 Duffey PH, Tretbar HC, Jarkowski TL. Giant cells in bone marrows in patients on high-dose fluoride treatment. *Archives of Internal Medicine* 75 745-747 1971.
- 44 Jones CA, Callahan MF, Huberman E. Sodium fluoride promotes morphological transformation of Syrian hamster embryo cells. *Carcinogenesis* 9 2279-2284 1988.
- 45 Lasne C, Lu YP, Chouroulinkov I. Transforming activities of sodium fluoride in cultured Syrian hamster embryo and BALB/3T3 cells. *Cell Biology and Toxicology* 4 (3) 311-324 1988.
- 46 Yiamouyiannis J, Burk D. Fluoridation and cancer. *Congressional Record* July 21 1975 pp H7172-H7176.
- 47 Yiamouyiannis J, Burk D. Cancer from our drinking water? *Congressional Record* December 16 1975 pp H12731-H12734.
- 48 Yiamouyiannis J, Burk D. Fluoridation and cancer: age-dependence of cancer mortality related to artificial fluoridation. *Fluoride* 10 102-123 1977.
- 49 Yiamouyiannis J. No studies by the US National Cancer Institute to investigate the possible carcinogenicity of fluoridation. Hearings before a Subcommittee of the Committee on Appropriations, House of Representatives, 94th Congress, Second Session 1976.
- 50 Hoover RN. The National Cancer Program (Part 2. Fluoridation of Public Drinking Water), Hearing before a Subcommittee of the Committee on Government Operations, 95th Congress, 1st Session, September 21 and October 12 1977, GPO 99-316-0: 80-82.
- 51 Oldham PD, Newell DJ. Fluoridation of water supplies and cancer. *Applied Statistics* 26 125-135 1977.
- 52 Kinlen L, Doll R. Fluoridation of water and cancer mortality in the US. *Lancet* 1300-1302 June 18 1977.
- 53 Dimenti B. Fluoride in drinking water. Toxic substances information. Virginia State Department of Health 1980 41 pp.
- 54 Yiamouyiannis J. Cancer mortality and fluoridation. *Lancet* January 21 150 1978.
- 55 Yiamouyiannis J. The National Cancer Program (Part 2. Fluoridation of Public Drinking Water), Hearing before a Subcommittee of the Committee on Government Operations, 95th Congress, 1st Session, September 21 and October 12 1977, GPO 99-316-0: 3-10, 61-72, 310-318.
- 56 Austin DF. Analyses testing the hypothesis that fluoride in drinking water is related to cancer in humans. Memorandum dated October 21 1975 to Chief, Family Services Section, State of California. In: The National Cancer Program (Part 2. Fluoridation of Public Drinking Water), Hearing before a Subcommittee of the Committee on Government Operations, 95th Congress, 1st Session, September 21 and October 12 1977, GPO 99-316-0: 394-399.
- 57 Kinlen L. Cancer incidence in relation to fluoride level in water supplies. *Community Health* 6 69-74 1974. (See also: Kinlen L. Transcript of testimony in Paul W Aikenhead v Borough of Westview No. GD 4585-78, Common Pleas of Allegheny County, Pennsylvania 1978 pp 29-30.
- 58 Knutson JW. An evaluation of the Grand Rapids fluoridation project. In: *Fluoride Drinking Waters* 1962 pp 213-217.
- 59 The National Cancer Program (Part 2. Fluoridation of Public Drinking Water). Hearing before a Subcommittee of the Committee on Government Operations, 95th Congress, 1st Session, September 21 and October 12 1977, GPO 99-316-0. p 319.
- 60 Toft J. *Sodium fluoride: individual animal tumor pathology table (mice)*. Battelle Memorial Institute, Columbus OH 1989 (February 23).
- 61 Persing R. *Sodium fluoride: individual animal tumor pathology table (rats)*. Battelle Memorial Institute, Columbus OH 1989 (April 11).
- 62 Procter and Gamble. Carcinogenicity studies with sodium fluoride. Presented at the National Institute of Environmental Health Sciences July 27 1985.
- 63 Dose determination and carcinogenicity studies of sodium fluoride in Crl:CD-1 mice and Crl:CD(Sprague Dawley)BR rats. In: *Review of Fluoride: Benefits and Risks. Report of the Ad Hoc Committee on Fluoride of the Committee to Coordinate Environmental Health and Related Programs*. US Public Health Service, 1991 pp 74 and D1-D7.

- 64 Maurer JK, Cheng MC, Boysen BG, Anderson RL. Two-year carcinogenicity study of sodium fluoride in rats. *Journal, National Cancer Institute* 82 1118-1126 1990.
- 65 Hoover RN, Devesa S, Cantor K, Fraumeni JF Jr. Time trends for bone and joint cancers and osteosarcomas in the Surveillance, Epidemiology and End Results (SEER) Program, National Cancer Institute. In: *Review of Fluoride: Benefits and Risks, Report of the Ad Hoc Committee on Fluoride of the Committee to Coordinate Environmental Health and Related Programs*. US Public Health Service, 1991 pp F1-F7.
- 66 Cohn PD. *A brief report on the association of drinking water fluoridation and the incidence of osteosarcoma among young males*. New Jersey Department of Health, Trenton NJ November 8 1992.
- 67 Hrudey SE, Soskolne CL, Berkel J, Fincham S. Drinking water fluoridation and osteosarcoma. *Canadian Journal of Public Health* 81 415-416 1990.
- 68 Mahoney MC, Nasca PC, Burnett WS, Melius JM. Bone cancer incidence rates in New York State: Time trends and fluoridated drinking water. *American Journal of Public Health* 81 475-479 1990.
- 69 McGuire SM, Venable ED, McGuire MH *et al*. Is there a link between fluoridated water and osteosarcoma? *Journal of the American Dental Association* 122 39-45 1991.
- 70 Freni SC, Gaylor DW. International trends in incidence of bone cancer are not related to drinking water fluoridation. *Cancer* 70 611-618 1992.
- 71 Yiamouyiannis J. *Fluoride, The Aging Factor* (2nd Ed). Health Action Press, Delaware 1986 pp 63-69.
- 72 Mason TJ, McKay FW. *Cancer Mortality by County: 1950 to 1969*. NIH publication no. 74-615, US National Cancer Institute 1974.
- 73 Hoover RN, Devesa S, Cantor K, Lubin JH, Fraumeni JF Jr. Fluoridation of drinking water and subsequent cancer incidence and mortality. In: *Review of Fluoride: Benefits and Risks, Report of the Ad Hoc Committee on Fluoride of the Committee to Coordinate Environmental Health and Related Programs*. US Public Health Service, 1991 pp E1-E51.
- 74 Gray AS. Fluoridation: Time for a new baseline? *Journal of the Canadian Dental Association* 53 763-765 1987.
- 75 Information supplied by N Brugge from official sources, January 1993.
- 76 Martin B. *Scientific Knowledge in Controversy: The Social Dynamics of the Fluoridation Debate*. State University of New York Press, Albany NY 1991 pp 296-306.
- 77 Schlesinger ER, Overton DE, Chase HC, Cantwell KT. Newburgh-Kingston caries-fluorine study. XIII. Pediatric findings after ten years. *Journal of the American Dental Association* 52 296-306 1956.
- 78 Caffey J. On fibrous defects in cortical walls: their radiologic appearance, structure, prevalence, natural course, and diagnostic significance. In: Levin SZ (Ed). *Advances in Pediatrics*. Interscience Publishers, New York 1955.
- 79 *Drinking Water and Health*. National Academy of Sciences, 1977 pp 388-389.
- 80 Kranwar KC *et al*. *In vitro* inhibition of testosterone synthesis in the presence of fluoride ions. In: *IRCS Medical Science Library Compendium* Vol.11 1983 pp 813-814.
- 81 Bucher JR, Hejtmancik MR, Toft JD *et al*. *Interpretations and conclusions on the National Toxicology Program's rodent carcinogenicity studies with sodium fluoride*. 1990 14pp.
- 82 Knox EG. *Fluoridation of Water and Cancer: A Review of the Epidemiological Evidence*. Her Majesty's Stationery Office, London 1985 116pp.
- 83 Transcript of testimony of Richard Doll in *McCull vs Strathclyde Regional Council*, Scottish High Court in Edinburgh, 1982 pp 19259-19261.
- 84 Shupe JL, Bruner RH, Seymour JL, Alden CI. The pathology of chronic bone fluorosis: A review. *Toxicologic Pathology* 20 274-285 1992.
- 85 Klein W, Kocsis F, Wottawa A. DNA repair and environmental pollutants. *Zeitschrift für Angewandte Bader und Klimaheilkunde* 24 218-223 1977.
- 86 Taylor A, Taylor NC. Effect of fluoride on tumor growth. *Proceedings, Society for Experimental Biology and Medicine* 119 252-255 1965.
- 87 Gibson SLM. Effects of fluoride on immune system function. *Complementary Medical Research* 6 111-113 1992.