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FLUORIDE
QUARTERLY REPORTS

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ABSTRACTS

FLUORIDATION AND BONE CANCER

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The NTP (National Toxicology Program) fluoride/cancer study of rats and mice (1) found a statistically significant dose-related increase of osteosarcoma incidence in male rats and, in addition, found fluoride correlations with thyroid follicular cell adenomas, oral and nasal squamous dysplasia, a rare type of liver cancer (hepatocholangiocarcinoma), and, as might have been expected, extensive osteosclerosis. Following this, the Public Health Service, under Dr Hoover *et al*, reviewed the limited SEER epidemiological data which also showed a significant association of water fluoridation with osteosarcoma incidence among males under 20 years of age (2). However, the meaning of this association was questioned by the PHS because of the apparent absence of a linear trend of a putative association over time of which water supplies were fluoridated. Despite this question, it is clear from the data that osteosarcoma in young men had increased over time and that this increase was greater in fluoridated areas. Also, a New York State study, excluding New York City, attempted to analyze its hospital and population data in regard to bone cancer incidence since the 1950s (3). However, due to a change in diagnostic classification from body site (*i.e.*, simply, "bone cancer") to cell type (osteochondroma, Ewing's sarcoma, and osteosarcoma) in the mid-1970s, the true change in incidence of osteosarcoma cannot be calculated. Despite the fact that osteosarcoma is rare (2.9 cases per million people on average annually in New Jersey), it is the most common primary malignant tumor of bone and is one of the principal cancers of childhood. Dr Cohn therefore thought it appropriate to survey its incidence in New Jersey relative to water fluoridation (4).

In his executive summary, Dr Cohn reports his findings of a strong statistical association between water fluoridation and osteosarcoma in young men but points out that the total number of cases is small and that he obtained no data concerning individual residence history, average water ingestion, use of dental fluoride supplements, exposure to other carcinogens, or family cancer history. For these reasons Dr Cohn advises that the results be interpreted cautiously. However, health decisions most often must be made on data which, from the viewpoint of pure science, are in one way or another incomplete. This is inherent in the practice of medicine.

Tables of the study results are reproduced on the following pages.

It should be noted that twelve cases of osteosarcoma were diagnosed among males under 20 in a three county area with the greatest prevalence of fluoridation. Of these, 2 were of age 0-9 and 10 were of age 10-19 years. The rate ratio of incidence in fluoridated *vs* non-fluoridated municipalities in the three county area was 5.1 (95% CI 2.7-9.0)*. Among 10-19 year old males in those three counties, the ratio rate was 6.9 (95% CI 3.3-13). No other age/sex

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* CI = Confidence Interval

groups exhibited significant association with fluoride. Thus it can been seen that, for these populations, the chance of osteosarcoma for males age 10-19 years was 6.9 times higher in the fluoridated municipalities.

As noted by Dr Cohn, the etiology of osteosarcoma has not been established. The fact that rapidly growing bone in adolescent males is most susceptible to the development of osteosarcoma suggests that fluoride, which is known to be toxic to bones and a potent enzyme inhibitor, may act as a cancer

Table 1. Age-/sex-specific osteosarcoma incidence in fluoridated vs non-fluoridated municipalities in seven counties in the central New Jersey study area. Number of cases (1979-1987), population and average annual incidence rate (cases per million), all races; NJDOH, 1992.

Sex	Age		Cases	Population	Rates
Males	0-9				
		Fluoridated	2	48,129	4.6
		Non-fluoridated	1	102,123	1.0
	10-19				
		Fluoridated	**10**	**62,990**	**17.6**
		Non-fluoridated	**7**	**151,384**	**5.1**
	20-49				
		Fluoridated	5	141,439	3.9
		Non-fluoridated	5	348,570	1.5
	50-69				
		Fluoridated	0	65,126	0
		Non-fluoridated	7	161,459	4.8
	70+				
		Fluoridated	1	21,614	5.1
		Non-fluoridated	4	48,649	9.1
Females	0-9				
		Fluoridated	0	45,936	0
		Non-fluoridated	2	103,462	2.1
	10-19				
		Fluoridated	3	61,533	5.4
		Non-fluoridated	5	145,790	3.8
	20-49				
		Fluoridated	2	152,173	1.4
		Non-fluoridated	5	362,616	1.5
	50-69				
		Fluoridated	1	76,461	1.4
		Non-fluoridated	2	182,912	1.2
	70+				
		Fluoridated	5	37,634	14.7
		Non-fluoridated	4	77,708	5.7

promoter during this narrow window of susceptibility. Given this, the available SEER epidemiologic data may be more significant than appreciated by the PHS which discounted the observed fluoride/osteosarcoma correlation on the basis of the absence of a linear trend of association with duration of time the water supplies were fluoridated. However, if fluoride acts as a cancer promoter, rather than an initiator, the duration/latency assumption is not warranted.

Table 2. Age-/sex-specific osteosarcoma incidence in fluoridated vs non-fluoridated municipalities in Mercer, Middlesex, and Monmouth Counties. Number of cases (1979-1987), population and average annual incidence rate (cases per million), all races; NJDOH, 1992.

Sex	Age		Cases	Population	Rates
Males	0-9				
		Fluoridated	2	38,654	5.7
		Non-fluoridated	1	46,708	2.3
	10-19				
		Fluoridated	**10**	**50,297**	**22.0**
		Non-fluoridated	**2**	**67,678**	**3.2**
	20-49				
		Fluoridated	4	115,367	3.8
		Non-fluoridated	2	153,713	1.4
	50-69				
		Fluoridated	0	51,853	0
		Non-fluoridated	2	66,607	3.3
	70+				
		Fluoridated	0	16,930	0
		Non-fluoridated	3	18,478	18.0
Females	0-9				
		Fluoridated	0	36,956	0
		Non-fluoridated	0	44,247	0
	10-19				
		Fluoridated	3	48,976	6.8
		Non-fluoridated	3	65,120	5.1
	20-49				
		Fluoridated	0	122,936	0
		Non-fluoridated	1	157,545	0.7
	50-69				
		Fluoridated	1	60,427	1.8
		Non-fluoridated	1	74,846	1.4
	70+				
		Fluoridated	4	29,068	15.2
		Non-fluoridated	3	28,524	11.6

In the context of the strong correlation of fluoride to osteosarcoma in male rats in the NTP study and the strong epidemiologic evidence of osteosarcoma incidence increase in young male in the US, especially in fluoridated communities, this report from New Jersey adds considerable weight to the probability that fluoride does indeed increase the risk of osteosarcoma among males.

Furthermore, fluoridation/caries studies of the past two decades (5-7), including the latest National Institute of Dental Research study (7), indicate that caries reduction in U.S. schoolchildren is *not* significantly correlated with fluoridation status. Therefore, given that osteosarcoma is potentially fatal and caries is not, and that other documented studies show fluoride-related increases in hip fractures, dental fluorosis, and other health damaging effects, it would be wise to cease all artificial fluoridation. Anyone who chooses to give their children additional fluoride in spite of all these risks would still be free to do so. I can think of no other agent with this degree of risk which is mandated by the PHS to be added to our food or water. The decision to use the agent should be left to the individual and his/her health advisor.

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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

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"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 sub-commitee 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 carcino-genicity, or lack of carcinogenicity, of this substance is a question which remains unanswered" (59) and his subcommitee 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 definitve conclusions about the role of fluoridaton 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 nonfluoridatedd 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 after1965 (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
	1973-1980	1981-1987	to 1981-1980
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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PREVALENCE OF. ENDEMIC FLUOROSIS WITH GASTROINTESTINAL MANIFESTATIONS IN PEOPLE LIVING IN SOME NORTH-INDIAN VILLAGES

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SUMMARY: Numerous reports on epidemiological surveys of skeletal and dental fluorosis exist, but information is quite limited on non-skeletal manifestations of fluoride toxicity. The present study was conducted to assess the prevalence and severity of non-skeletal manifestations, especially gastrointestinal disturbances, in an area of skeletal and dental fluorosis.

The subjects, numbering 1958 inhabitants belonging to 489 families residing in four endemic villages of Faridabad District of Haryana State, were interviewed on health complaints. The information was recorded in a precoded questionnaire. Every drinking water source was analysed for fluoride content. This led to the identification of "safe" (fluoride 1 ppm or less) and "contaminated" (fluoride above 1 ppm) sources of water.

Results revealed that among the subjects were people affected with: 1) Dental fluorosis (58%), 2) Skeletal fluorosis (27%), 3) Non-skeletal manifestations (41%) and 4) Gastrointestinal complaints (26%). Those affected were consuming water contaminated with fluoride ranging from 0.25-8.00 ppm. Among the total of 78 sources of water, 20 were "safe" while the remaining 58 were more contaminated with fluoride from natural sources.

It is concluded that in an endemic zone, where the inhabitants are consuming water of high fluoride content, the occurrence of gastrointestinal complaints - viz., loss of appetite, nausea, abdominal pain, flatulence, constipation and inter- mittant diarrhoea - is one of the early warning signs of fluoride toxicity and fluorosis. When water with negligible amounts of fluoride (safe water) is provided, the complaints disappear within a fortnight.

Key words: Dental fluorosis; Endemic fluorosis; Epidemiology; Faridabad, Haryana (India); Gastrointestinal disturbances; Non-ulcer dyspepsia.

Introduction

Endemic fluorosis is a form of chronic fluoride intoxication resulting from ingestion of excessive quantities of fluoride through drinking water. This form of chronic intoxication was first described in one of the southern States of India in 1937 (1,2). Cases of endemic fluorosis have been reported sporadically from almost all parts of the world, particularly from China (3), Japan (4), South Africa (5), North Africa (6), Argentina (7), the Persian Gulf (8), Saudi Arabia (9), United States of America (10,11), Canada (12) and Europe (13,14). Shortt et al (1,2) were the pioneers in recognizing the disease, from cases of dental and skeletal fluorosis among residents of Nellore District in Andhra Pradesh. Subsequently the condition was associated with ingestion of fluoride in drinking water. Pandit et al (15) made a comprehensive study in this area dealing with the etiological aspect. Daver (16)

reported endemic fluorosis from Hyderabad. Khan and Wig (17) reported chronic fluoride toxicity with bone affliction in Punjab. Siddiqui (18) noted symptoms of fluoride toxicity in immigrants within 1-4 years of entering an endemic village. Singh *et al* have reported extensively on dental, skeletal and neurological aspects of the disease (19,20). Anand *et al* (21) described cases of endemic fluorosis in the Delhi region. Jolly *et al* (22,23) studied dental fluorosis in schoolchildren and tried to correlate the incidence with the water fluoride level.

The large quantity of drinking water consumed in hot arid climates is supposed to contribute to a higher daily intake of fluoride resulting in incidence of clinical fluorosis (24,25). The work of Brouwer *et al* indicated that in the hot climate of Senegal both dental and skeletal fluorosis are more prevalent and severe than would be expected from the fluoride concentration in drinking water (26). Fisher *et al* (27) have reported a case of spinal cord compression with paraplegia as a result of endemic skeletal fluorosis. An epidemiological study by Evans (28) reported the dependence of dental fluorosis on fluoride exposure during the critical period of tooth development.

The major pathway by which fluoride enters the circulation is by absorption from the gastric and duodenal mucosa (29). Unlike most substances, fluoride can be absorbed in appreciable amounts from the stomach (30), which is why gastric and intestinal disorders are noticed in most of the cases of osteofluorosis (31). Gastrointestinal problems, most commonly abdominal pain, vomiting, nausea and anorexia, have recently been reported in fluorosis patients and patients on sodium fluoride therapy (32). The effect of a single dose of fluoride was tested in 12 healthy male and female volunteers who underwent endoscopies two hours after consuming fluoride (33). The stomach was videotaped and examined. Mucosal injury and structural damage were observed. However, no epidemiological survey on non-skeletal manifestations of fluorosis, with a focus on gastro-intestinal disturbances, has appeared so far. The present study was undertaken to assess the prevalence and severity of skeletal and dental fluorosis, and accompanying non-skeletal manifestations with gastrointestinal disturbances, among the people of four villages in Faridabad District of Haryana State.

Material and Methods

The four villages Samaypur, Karnera, Sikrona and Bhanakpur of the Faridabad District were chosen randomly for survey work, because large numbers of patients from that area with backache, joint pain and pain in the neck and hip region, later diagnosed as cases of skeletal fluorosis, had visited the Outpatients Department of the All India Institute of Medical Sciences Hospital. A door to door survey with face-to-face interviews was carried out. The information collected was entered on a pre-coded questionnaire. Health complaints related to dental fluorosis, skeletal fluorosis, and non-skeletal manifestations, including gastrointestinal complaints, were recorded.

The teeth were examined for characteristic mottling and pigmentation, *viz.,* yellow-white patches, brown streaks or black patches on the enamel surface, and pitted, perforated or chipped-off enamel. Information was recorded on complaints of severe pain and the rigidity of back-bone, joints and neck and hip region through a set of simple tests illustrated in the Figure. Besides non-skeletal manifestations, *viz.,* aches and stiffness of muscles, muscle weakness, tingling sensation in hands

and feet, polydypsia and polyuria were also recorded. Complaints of abdominal pain, constipation, intermittent diarrhoea, bloated feeling, loss of appetite, feeling of nausea, and mouth sores were recorded under gastrointestinal disturbances.

Water samples were collected from all sources from each village. Fluoride estimation was done on an ION 85 ION ANALYZER (Radiometer, Copenhagen). The main sources of drinking water in these villages are open wells, hand pumps and municipal supply.

FIGURE LEGENDS

Normal healthy individual:

A Can bend body and touch the floor/toes.
C Can touch chest with chin.

E Can stretch hands, fold arms and touch back of head.

Fluoride toxicity manifestation:

B Unable to bend without folding knees.
D Unable to bend neck - touching chest with chin not possible.
F Unable to stretch hands, fold arms and and touch back of head.

A   B

C   D

E   F
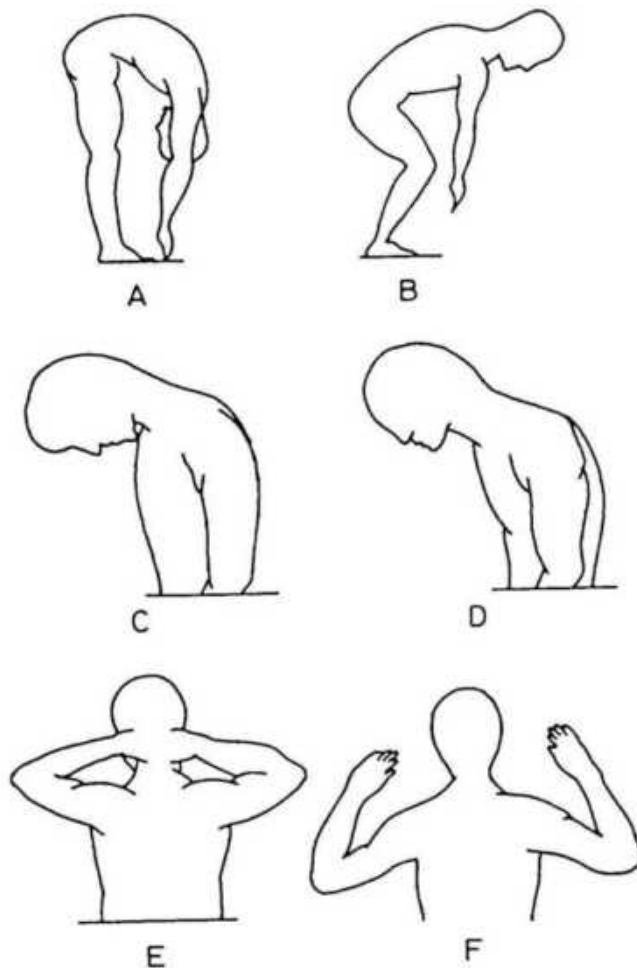
Credit V. K. Desai

Results and Discussion

The results are summarized in Tables 1 and 2

TABLE 1

Water quality and health status in four villages of Faridabad District

Village:		SAMAYPUR		KARNERA		SIKRONA		BHANAKPUR	
Total families surveyed		89		79		99		222	
Total population surveyed		288		315		518		837	
Total no. and percent of cases:									
of dental fluorosis		190	65.9%	275	87%	317	61%	353	42%
with skeletal fluorosis		163	56.6%	135	42.8%	94	18%	141	16.8%
with non-skeletal manifestations		184	63.9%	214	67.9%	135	26%	264	31.5%
with gastrointestinal manifestations		151	52.4%	155	49%	61	11.7%	143	17%
Total no. of water sources		36		32		6		4	
No. of safe water courses		11		4		2		3	
Fluoride content of water:	Min.	0.25 ppm		0.3 ppm		0.3 ppm		0.7 ppm	
	Max.	8.0 ppm		7.0 ppm		5.4 ppm		1.6 ppm	
	Mean	3.2 ppm		3.7 ppm		2.5 ppm		1.0 ppm	

TABLE 2

Summary of observations

		Number	Percentage
No. of villages:	4		
No. of families:	489		
Total population surveyed	1953		
Total no. of cases with dental fluorosis		1135	58
Total no. of cases with skeletal fluorosis		533	27
Total no. of cases with non-skeletal manifestations		797	41
Total no. of cases with gastrointestinal manifestations		510	26
Total no. of water sources:		78	
Total no. of safe water sources		20	
Fluoride content in water: Minimum		0.25 ppm	
Maximun		8.0 ppm	

Dental fluorosis

Mottled enamel or dental fluorosis is a well recognized entity (34,35) and one of the overtly visible signs of excessive intake of fluoride during the period of teeth eruption. In this survey the overall prevalance of dental fluorosis in the four villages was 58%. Fluoride concentration in drinking water ranged between 0.25 and 8.0 ppm. The highest prevalence of dental fluorosis, 87%, was found in Karnera village where the drinking water fluoride was in the range of 0.3 - 7.0 ppm.

Ray et al (36) reported 28.21% dental fluorosis in a rural area of Varanasi. Desai et al (37) observed 35.3% dental fluorosis among 4544 tribals from 24 villages. In a locality near Punjab, where water fluoride concentration was 9.7 ppm, 70.7% of the population had dental fluorosis (22). In the present survey the prevalence of dental fluorosis was 42% where the upper limit of fluoride in drinking water sources was 1.6 ppm, which is close to the upper permissible limit of 1.0 ppm (Table 1). Manji et al (38) found high prevalences and severity of dental fluorosis in Kenya at low water-fluoride levels 0.1-1.0 ppm. Smith and Hodge (39) reported that 2 ppm fluoride caused mottled enamel. Ray et al (36) observed dental fluorosis at 0.4 ppm fluoride in drinking water. Brouwer et al (26) have shown dental fluorosis in children in Senegal where water-fluoride ranged from 0.1 to 7.4 ppm, with mild dental fluorosis prevalence of 68.5% at 1.0 ppm. When fluoride content exceeded 4 ppm, dental fluorosis prevalence reached 100%.

Skeletal fluorosis

The present survey revealed that overall prevalence of cases of skeletal fluorosis in the four villages, verified through 3 physical tests, was 27% (Table 2 and Figure). The results clearly showed (Table 1) that the incidence of skeletal fluorosis was dependent on fluoride concentrations in drinking water. These observations are in accordance with the observations made earlier by Jolly et al (22,23), who reported 2.4% skeletal fluorosis prevalence at drinking water fluoride concentrations of 0.9-2.5 ppm and 70.7% prevalence at concentrations of 6.0-16.2 ppm. Singh and Jolly (40), on the basis of extensive epidemiological surveys, found that crippling fluorosis resulted from continuous daily intake of 20-80 mg fluoride for 10-20 years. However, in India skeletal fluorosis has been reported at very low levels of fluoride intake for shorter duration (20,22). In some studies in tropical countries reviewed by the Royal College of Physicians (15,23,41) relatively marked osteofluorotic symptoms were found with drinking water fluoride levels of 1.0-3.0 ppm.

An Indian report in a 1970 WHO publication indicated that one can be afflicted with fluorosis by drinking water contaminated with 20 ppm fluoride for ten years (40). The fact remains that even 2 ppm fluoride contaminated water consumed for two years can cause crippling fluorosis, if the calcium content of the water is low and alkalinity is high (42). A recent epidemiological survey conducted by Teotia and Teotia (1990) showed that dental and skeletal fluorosis occur in rural areas of Uttar Pradesh where the fluoride content of drinking water is only 0.6 ppm. They also reported that consuming fluoride over a period of six months to one year is adequate for the onset of manifestations of skeletal fluorosis (43,44).

It can be concluded that fluoride in drinking water is an important disease factor. In fact, skeletal fluorosis and its associated manifestations can develop following ingestion of fluoride within "permissable" limits. This observation suggests that fluoride can enter the body from other sources besides drinking water and that the effects can be aggravated by other factors (15,20,41,43) *e.g.* low calcium, high water alkalinity, and dietary deficiency of calcium and vitamin C besides the hormonal profile.

Non-skeletal manifestations

In the present survey the overall incidence of non-skeletal manifestations in the four villages was 41% (Table 2). The maximum prevalence was 67.9%, observed when the mean value of fluoride in drinking water was 3.7 ppm. A prevalence of 63.9% was observed when the mean water fluoride value was 3.2 ppm, and a prevalence of 26% at mean of 2.5 ppm. However, a 31.5% prevalence of non-skeletal manifestations was also observed at a mean water fluoride level of only 1.0 ppm (Table 1).

In Faridabad District, severe gastro-intestinal problems have been observed. The overall prevalence of non-ulcer dyspeptic symptoms in the four villages was 26%. The highest prevalence was found in one village which had 52.4% with gastrointestinal problems at fluoride levels ranging from 0.25 to 8.0 ppm. Waldbott (45) had also reported that 47% of fluorosis patients in Sicily were affected with gastrointestinal problems. The extent of fluoride absorption from the stomach has implications in that gastric acidity enhances both the absorption and the toxicity of fluoride (30). Susheela reported that gastro-intestinal complaints are an early warning sign of fluoride toxicity and fluorosis (46).

It has also been shown by Susheela and Das (47) that in rabbits subjected to oral administration of NaF at the dose of 10mg/kg body weight for a period of 24 months fluoride toxicity destroys the gastro-intestinal mucosa, *i.e.* causes loss of microvilli, loss of mucus, and surface abrasions due to epithelial cell degeneration. Susheela and Kumar (48) have also reported damage and abrasion of epithelial cells of mucosa of systems other than gastrointestinal, *viz.* vas deferens and ductuli efferentis of rabbits after oral administration of NaF at 10mg/kg body weight daily for varying time intervals. The authors also reported a significant reduction in mucus droplets in fluoride treated animal both in the gastrointestinal tract and vas deferens.

A recent study (32) on long term ingestion of fluoride by human patients from endemic areas and patients on sodium therapy for otosclerosis revealed non-ulcer dyspeptic symptoms in 70% of the subjects. In upper gastrointestinal endoscopy, petechiae, erosion, and erythema were seen in all patients compared to normal healthy controls. The biopsy material obtained, when examined under the scanning electron

microscope, revealed mucosal abnormalities. The observation suggests that gastrointestinal complaints comprising non-ulcer dyspeptic symptoms in endemic areas can be caused by ingestion of excess fluoride. We have observed that, when such patients revert to safe drinking water either in an endemic area or while in hospital, they are relieved of the dyspeptic symptoms and complaints within 2-3 weeks.

This is one of the first reports revealing the results of fluoride toxicity after a systematic epidemiological survey and water quality analysis. It provides evidence, supported by laboratory and other clinical investigations including endoscopy, which suggests that gastrointestinal complaints are early warning signs of fluoride toxicity and fluorosis in an endemic area.

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EFFECT OF DIETARY FLUORINE ON HISTOPATHOLOGICAL CHANGES IN CALVES

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SUMMARY: To investigate the pathological effects of subclinical levels of dietary fluorine (F) on twenty male Karan Fries calves aged about 6-8 months, the experimental calves were given diets comprised of concentrate mixture and green maize (50:50 for first 3 months and 40:60 during the later phase). For the preparation of mineral mixture (incorporated in the concentrate mixture), two sources of phosphorus supplements, viz. dicalcium phosphate and rock phosphate, either as such or fortified with sodium fluoride, were used. The resultant dietary F levels in the four groups were 7, 79, 132, and 191 ppm. The liver and kidney showed mild degenerative and inflammatory changes. Bone exhibited periosteal hyperostosis, compactness of bony tissues and osteopetrotic changes, indicating initial alterations in bony tissues resulting from pre-clinical conditions of dietary F excess.

Key words: Calves; Degenerative; Histopathology; Inflammatory; Kidney; Liver; Osteopetrotic; Periosteal hyperostosis; Phosphorus supplements; Subclinical.

Introduction

Dairy cattle are most sensitive to fluorine (F) intake. Mineral mixtures having natural rock phosphate as a phosphorus supplemental source contain high F levels which may adversely affect cattle performance. Defluorinating procedures are expensive and the technology is neither fully developed nor routinely followed. The levels of defluorination are also not ascertained. Rock phosphate used in the present study contained 15000 ppm F and its incorporation in concentrate mixture led to a level of 132 ppm F in the diet. Lower and higher dietary F levels were maintained by adding sodium fluoride (NaF) to dicalcium phosphate and rock phosphate, respectively. In cattle, the "safe" fluorine level from rock phosphate is 60 to 100 ppm and from NaF is 40 ppm (1). But reports (2,3) indicate that even the recommended safe level of dietary F does not protect dairy cattle against severe chronic fluoride poisoning. Adequate information is available on clinical aspects of fluorosis. However, information is scarce regarding tissue injury at moderate levels of F fed for a short period resulting in no clinical manifestations. Therefore the present study was undertaken to investigate the effect, if any, of subclinical levels of excess dietary fluorine upon internal organs and hard tissues.

Materials and Methods

Twenty male Karan Fries (Tharparkar x Holstein) calves aged 6-8 months were divided into four equal groups in a randomized block design. The animals were fed on diets comprised of concentrate mixture and green maize in the ratio of 50:50 for or up to three months. Thereafter, the ratio was changed to 40:60 for the remaining one and a half months experimental period. Concentrate mixtures were formulated using barley 40, groundnut cake 40, wheat bran 17 and mineral mixure 3 parts so as to supply 22 per cent CP and 72 per cent TDN. Composition of mineral mixtures differed only with respect to the source of phosphatic supplement used (see Table). Mineral mixtures of

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groups 1 and 2 contained dicalcium phosphate which was completely replaced by rock phosphate in groups 3 and 4. However, mixtures in groups 2 and 4 were also fortified with NaF in order to achieve the higher dietary F levels. The resultant F levels thus were 7, 79, 132 and 191 ppm in treatment groups 1 to 4, respectively. Composition of concentrate mixtures in the treatment groups were similar with regard to protein, energy and minerals and thus F was the only dietary variable in the present study. At the termination of the experiment the animals were sacrificed by giving intravenous injections of saturated solution of $MgSO_4$. Representative samples of various soft tissues (liver, kidney, spleen, heart and lungs) and thin slices of hard tissue (transverse section of anterior part of metatarsal bone measuring 2-4 mm in thickness) were collected in 10 per cent buffered formol saline (4). For decalcification of hard tissues, samples were put in formol nitric acid decalcifying solution (5). Thin tissue sections prepared following conventional procedures were stained with haematoxylin and eosin (4).

TABLE. Composition of mineral mixture (per 3 kg)

Treatment groups	Ingredients			
	Dicalcium* phosphate (kg)	Rock* phosphate (kg)	'F' added** (g)	Other*** minerals
1	1.65	-	-	+
2	1.65	-	16	+
3	-	1.65	-	+
4	-	1.65	16	+

*   Basal F levels in dicalcium phosphate and rock phosphate were
       0.018% and 1.5%, respectively.
**   Varied time to time depending upon DM requirement so as
       to supply 80 ppm additional F in the diet.
***   Chalk powder 0.3312 kg, $MgCO_3$ 0.09 kg, NaCl 0.90 kg and
       trace elements 0.0288 kg.

Results and Discussion

The animals in the experimental groups did not show any clinical manifestation of fluorosis during the period under observation. At postmortem, internal organs as well as bones did not reveal any alteration of significance. Microscopic examination of heart, lungs and spleen also did not indicate any significant tissue damage. However, liver, kidney and metatarsal bones exhibited some alterations.

In liver, structural changes were evident only in groups 3 and 4, *i.e.* at 132 and 191 ppm F. At lower dietary F intake, *i.e.* at 7 and 79 ppm F (Groups 1 and 2), there was no discernible effect on normal liver structure. At 132 ppm F, variable intensities of hydropic degenerative changes, particularly around the central vein suggestive of centrilobular necrosis, were evident. Mononuclear cell infiltration in portal triad areas (Figure 1) were also visible. The changes were more pronounced at 191 ppm F as the liver microsections presented moderate changes of centrilobular necrosis (Figure 2). In kidney, focal intertubular mononuclear cell infiltration was observed even at the 79 ppm level (Figure 3). Besides, at 132 ppm, atrophied glomeruli with more periglomerular space were noticed (Figure 4). More pronounced changes like periglomerular fibrosis and tubular nephrosis were observed at 191 ppm F level.

The changes exhibited initially around the blood vessels might be correlated with excessive F concentration in the blood. Consequently, extravasation of fluoride ions diffusing out in surrounding areas might be responsible for excessive tissue damage as well as mononuclear cell infiltration. In an early report by Phillips *et al* (6), hyaline degenerative changes in liver, kidneys and suprarenal gland have been described in heifers fed diets containing 1.25% rock phosphate. However, no significant tissue alterations were observed by Greenwood *et al* (7) in internal organs on feeding dairy cattle at 93 ppm F level for up to 7½ years. Since soft tissues retain only a small fraction of dietary F (8) it is likely that the structural alterations observed in the present study are consequent only to the vascular F extravasation rather than the tissue retention. Alterations observed in tissues in the present study were similar to those reported earlier (7-9).

Grossly, the bone surface was mostly smooth with no apparant alterations. However, in a few it lost its natural lustre and a roughened surface was evident. Microsections of metatarsal bones showed subperiosteal compactness and periosteal irregular borders. At 132 ppm F intake, periosteal proliferations indicating osteopetrotic changes were observed. These changes were more severe at the 191 ppm F level, indicated by increased roughening of the periosteal surface (Figure 5). In clinical fluorosis, structural alterations in hard tissues like bones (metacarpal, metatarsal, rib, mandible) and teeth have been reported. Changes like roughening of periosteal surface, osteoporosis, osteoblastic new bone formation on premorbid subperiosteal surface *etc.*, have been reported by many workers (10-12). In the present study, osteopetrotic changes and periosteal hyperostosis along with minimal gross lesions indicate only the initial changes that might have resulted from subclinical conditions of dietary F excess.

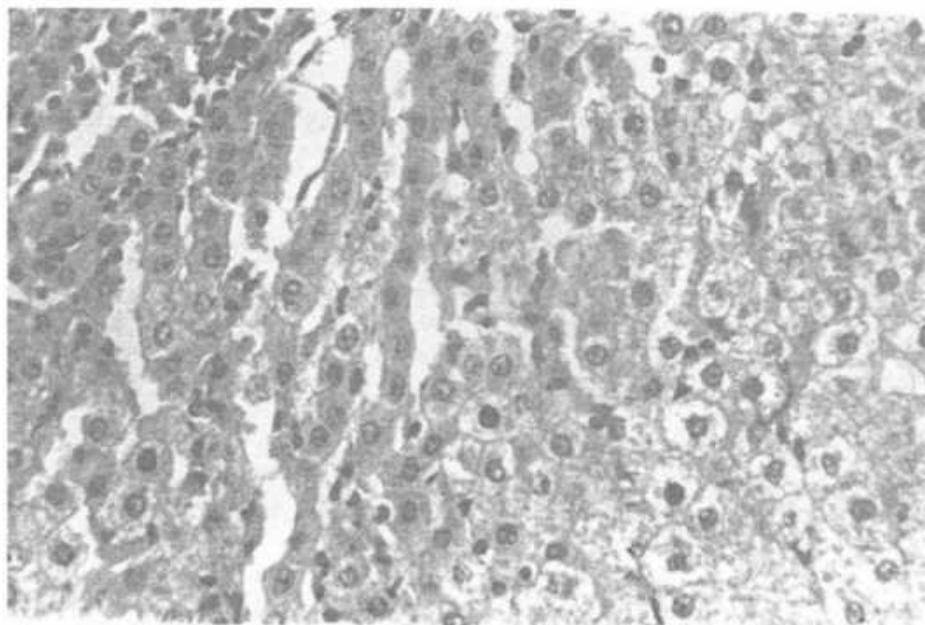FIGURE 1. Liver showing hydropic changes in the hepatic cells and slight mononuclear infiltration. HE X 280.
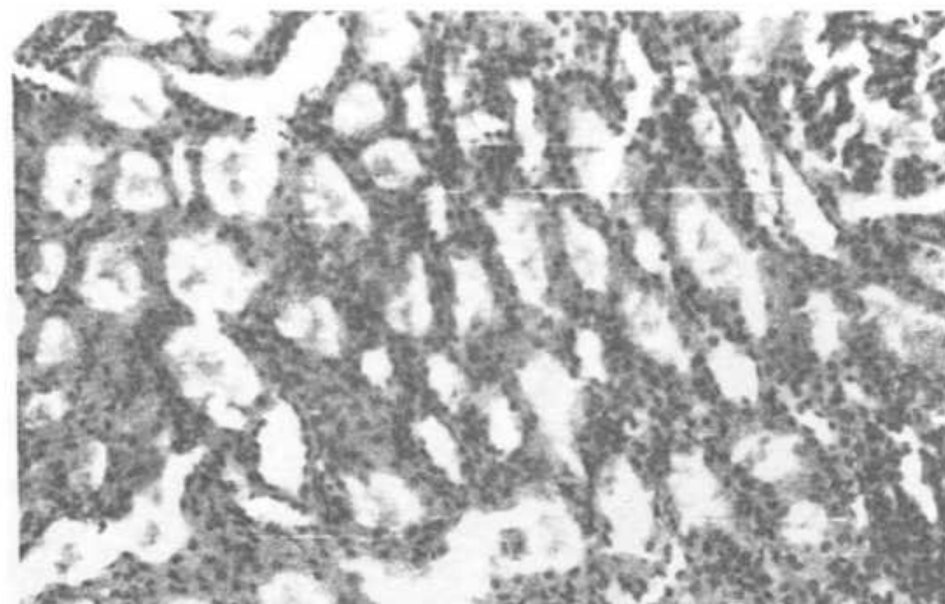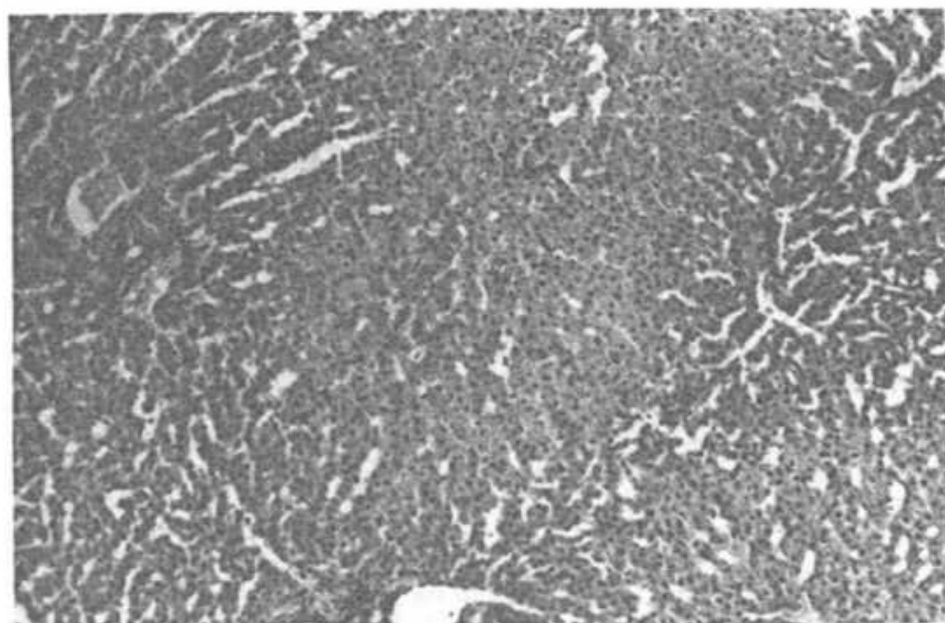
FIGURE 2 (upper). Liver showing mild centrilobular necrosis. HE X 70.

FIGURE 3 (lower). Kidney showing focal intertubular
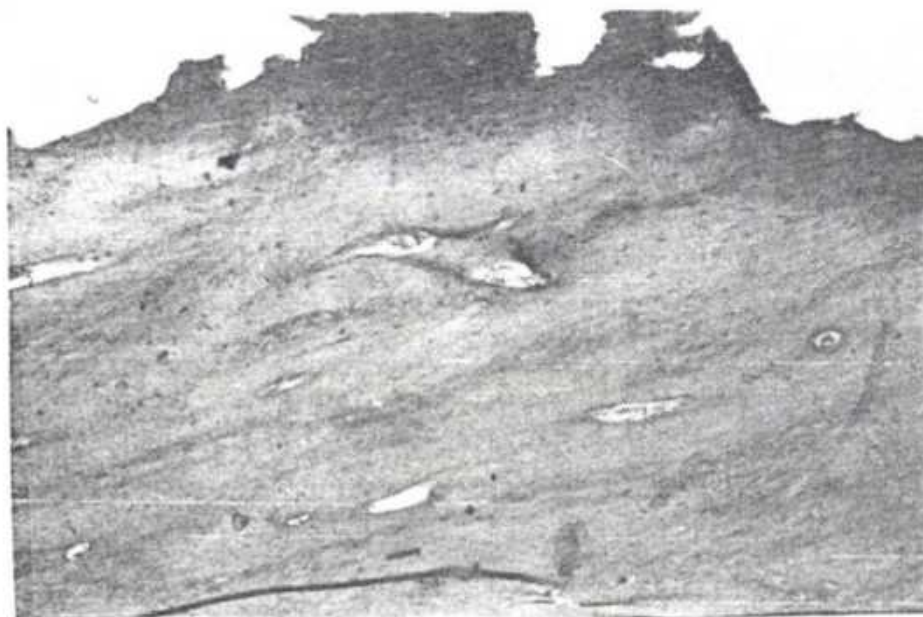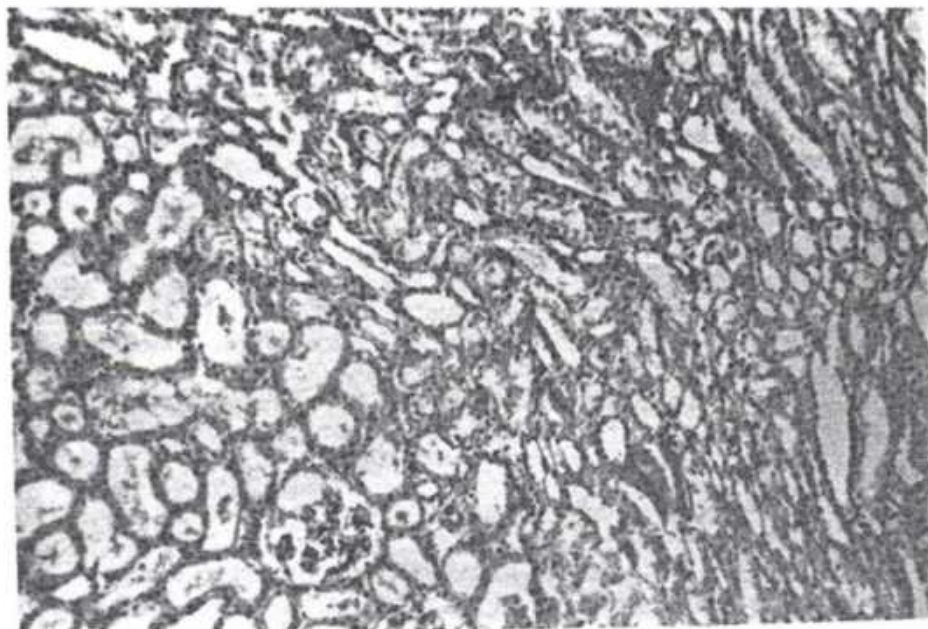mononuclear cell infiltration. HE X 280.

FIGURE 4 (upper). Kidney showing atrophied glomerulus. HE X 70.

FIGURE 5 (lower). Metatarsal bone showing
roughening of periosteal surface. HE X 70.

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PLASMA FLUORIDE LEVELS IN PRETERM BABIES

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SUMMARY: Plasma fluoride levels were determined in 25 term and 32 preterm babies. Venous blood samples were obtained within the first 48 hours of life and analyzed by the fluoride-ion selective electrode. Mean plasma fluoride levels in the term babies were significantly higher than in the preterm babies (92.47 ± 8.40 mg/L vs 57.74 ± 6.94 mg/L, $p < 0.001$). Plasma fluoride levels showed no correlation with gestational age and birth weight, respectively ($r = 0.33$, $p > 0.05$; $r = 0.30$, $p > 005$).

Key words: Babies; Plasma fluoride; Preterm babies.

Introduction

Fluoride intake has been considered to be an important factor for decreasing tooth decay in children (1). Some studies have purported to show that fluoride intake during pregnancy has a preventive effect on tooth decay of the baby (2-4). Knowing placental transfer of fluoride is also important for investigating this effect of fluoride. There is some disagreement, however, whether placental transfer of fluoride is active or passive (2). The aim of this study was to determine plasma fluoride levels in preterm babies and to investigate the effect of gestational age on such levels.

Material and Methods

Between June 1991 and August 1991, 25 term babies (Group I) which were born in the Obstetrics Clinic and 32 preterm babies (Group II) admitted to the Newborn Unit were included in this study. None of the mothers in either group had taken extra fluoride besides regular diet. Gestational ages of all babies were determined by Farr's Score and the mother's last menstrual period (5). None of the mothers in both groups had taken extra fluoride besides their regulat diet. Gestational ages of Group I babies ranged between 38-42 weeks (mean 39.7 ± 0.9 weeks) and birth weights between 2700-4300 g (mean 3498 ± 323 g). Gestational age of Group II babies ranged between 30-37 weeks (mean 32.2 ± 1.9 weeks) and birth weights between 1050-2800 g (mean 1725 ± 439 g). Birth weights of all the babies were appropriate for gestational age. The average age of the mothers of Group I babies was 27.3 years (range 19-38), and of Group II babies it was 25.5 years (range 18-32).

Two mililitres of venous blood were obtained from each baby within the first 48 hours of life and put into polyethylene tubes containing Na_2EDTA. The plasma derived after centrifuging the blood was stored at -20°C until the day of analysis. Plasma fluoride levels were measured by a fluoride-ion selective electrode (Orion Model 94-09) according to the method described by Kissa (6,7). This electrode was combined with an Ag/AgCl reference electrode (Orion Model 90-01). Cell potential was measured by ion analyzer (Orion Model 720PH/ISE Meter).

Statistical analyses were performed using the Mann-Whitney U and correlation tests.

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Results

All plasma fluoride levels are given in the Figure. Plasma fluoride levels ranged between 9.66-196.00 µg/L (mean 92.47 ± 8.40 µg/L) in Group I and 7.98-150.97 µg/L (mean 56.74 ± 6.95 µg/L) in Group II (see Table). The plasma fluoride levels showed a statistically significant difference between the two groups ($p < 0.001$).

Plasma fluoride levels showed no correlation with gestational age ($r = 0.33$, $p > 0.05$) and birth weight ($R = 0.11$, $p > 0.05$).

FIGURE. Plasma fluoride levels of the babies
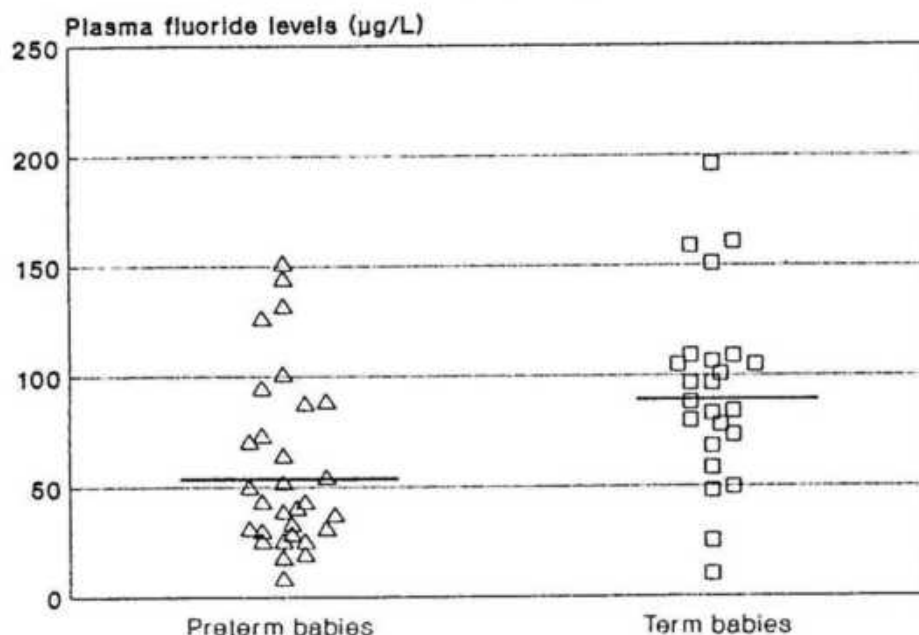

TABLE. Plasma fluoride levels of term and preterm babies

	Preterm babies n = 32 Mean ± SEM	Term babies n = 25 Mean ± SEM	P
Plasma fluoride levels (µg/L)	56.74 ± 6.95	92.47 ± 8.40	< 0.001

Discussion

Fluoride uptake by the skeletal system and teeth depends upon fluoride intake and absorption. Under normal conditions, fluoride accumulates in the skeletal system during life (8). The fluoride content of teeth also increases with age and the fluoride content of drinking water (8). Fluoride is also incorporated into the enamel of temporary teeth during the mineralization phase, which begins after four months of fetal life (9,10). Various studies have concluded that fluoride intake of the mother during pregnancy reduces tooth decay in babies (4,11,12). Caldera *et al* (2) reported that fluoride intake during the last trimester of pregnancy significantly increases plasma levels of fluoride in maternal and cord plasma at term. Dietary fluoride intake had little influence on either maternal or cord fluoride levels in the unsupplemented subjects.

Controversy still exists on whether placental transfer of fluoride is active or passive (2). Maternal plasma fluoride levels correlate well with cord plasma, suggesting that placental transfer of fluoride occurs with passive diffusion (2,13,14).

Fluoride levels of amniotic fluid are higher at term than in the second trimester. This finding has been explained in terms of higher fetal urinary excretion of fluoride at term due to lower sequestration of fluoride as the process of bone calcification becomes more complete (15). In our study, plasma fluoride levels of preterm babies were found to be significantly lower than those of term babies, which can be attributed to the low level of total body fluoride content and fluoride uptake of bone and teeth in preterm babies.

We suggest that plasma fluoride levels of pregnant women should be determined at various stages of gestation to help determine the reason for the low plasma fluoride levels in preterm babies.

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Research Report   115

FLUORIDE CONCENTRATIONS IN DENTINE AND
ACID-INDUCED DEMINERALIZATION *IN VITRO*

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SUMMARY: Human permanent teeth of known history with respect to fluoride exposure were split into crown and root portions and sections cut longitudinally near the mid-line. The sections were ground to about 80 microns thickness, and under the microscope a line was cut across the dentine at approximately right angles to the direction of the tubules in specific areas of crown and root. Sections were sandwiched between wax strips so that only cut edges were exposed to lactic acid 10% gelatine gels. The pH in most cases was about 5.4, and the exposure time was varied from 7 to 28 days. The extent of the penetration of the demineralization into the dentine and the degree of mineral loss were measured in contact microradiographs. Selected areas from microradiographed specimens were also examined by electron microscopy (EM). In other sections, a narrow strip of dentine weighing about 1 mg was removed parallel to the cut edge and the fluoride concentration determined in duplicate samples.

No consistent correlation was observed between fluoride levels in dentine over the range 50 - 2000 ppm F and the progression or extent of the demineralization, though there was a tendency for the highest fluoride concentrations in root dentine to be associated with the least penetration. EM studies confirmed the microradiographic findings.

Key words: Demineralization; Dentine; Fluoride; Root caries.

Introduction

In contrast to the extensive studies on the distribution of fluoride in enamel and its association with caries, remarkably little parallel work has been done on dentine. The realization that root caries is becoming a more common clinical problem has stimulated a recent surge of interest. The finding that in areas with fluoridated water less root caries has been observed (1-3) might be explained by a systemic "built in" protective effect of fluoride in dentine or cementum against demineralization (2), and in support of this is the report that acid solubility was inversely related to fluoride levels acquired systemically (4). Alternatively, fluoride in the environment of the tooth might encourage remineralization. Several studies have demonstrated this role in lesions of coronal and root dentine and cementum (5-11).

Further evidence for the influence of fluoride in dentine on lesion development comes from work in which fluoride, applied to the root dentine, caused retardation of demineralization *in vitro* (9,12-16).

Surprisingly little is known about the distribution of fluoride in dentine and the effects of fluoride ingestion on it. The most complete report showed the pattern of fluoride in dentine and cementum and the increases associated with ingestion of fluoride and with age (17). These results have been confirmed by others (18,19).

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The object of the present work was to test the hypothesis that the fluoride concentration naturally acquired in specific regions of root and crown dentine influenced the degree of demineralization of these regions when the demineralization was induced *in vitro* by acidified gels. Such gels have been reported to produce root surface lesions resembling histologically early carious lesions (20).

Materials and Methods

In order to provide a wide range of fluoride concentrations in dentine, human permanent molars and premolars were obtained from long-term residents of seven communities with fluoride levels in their water supplies ranging from <0.2 to 5.2 ppm. Only a limited number of such teeth were available to us. The teeth, which had been stored at -10°C, were subsequently rinsed in dilute ethanol at room temperature and separated into crown and root portions. Several longitudinal sections at a thickness of about 180 μm were cut near the mid-line from each tooth without embedding. These were ground to 80 μm ± 5 μm and stored in a humid

FIGURE 1. Diagrams showing the regions within sections of crown and root dentine which were removed for (A) demineralization studies and (B) fluoride determinations. The edges which were subsequently exposed to lactic acid gelatine gels are arrowed in A.
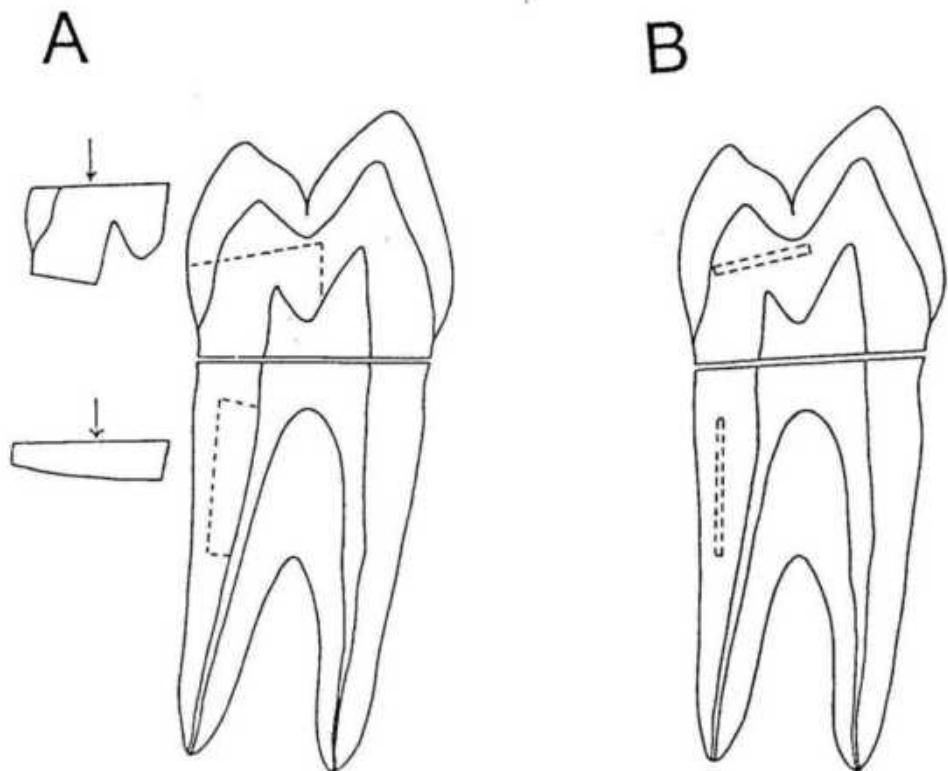
atmosphere at 4°C to prevent dehydration and shrinkage. Under the dissecting microscope straight cuts were made across the sections in specific regions of both crown and root (Figure 1A) at approximately right angles to the direction of the tubules.

Demineralization studies

Sections were sandwiched between 2 strips of pink modelling wax (2 x 6 cm) such that their cut "experimental" edges were precisely aligned with the long edges of the wax strip. Good seals were created around the sections. These procedures were carried out under the dissecting microscope. The identity of each section was coded on the overlying wax strip. The dentinal surfaces were exposed to lactic acid 10% undialyzed gelatine gels, the pH of which was 4.6 or 5.4 for the periods of 7, 12 and 28 days, after which time the wax strips were removed from the gel and rinsed under running water. The mean total fluoride concentration of these gels was 1.63 ppm. The sections were extracted from the separated strips and carefully cleared of any attached wax. They were mounted along with an aluminium step-wedge on a high resolution plate (Kodak HR, Type 1A). Contact microradiographs were prepared using a Hilger and Watts (Y33) X-ray generator, operating at 30 kV and 2.5 mA tube current with a target-specimen distance of 53 cm. The optimum exposure time was 1 hour. Up to 12 specimens were exposed on 1 plate. The plates were processed in a standardized manner. Microradiographs were examined under the light microscope, but the identity of each was unknown to the examiner. By means of a calibrated graticule in the eyepiece, estimates were made of the depths of both surface demineralization and the advancing boundary of radiolucency. One division of the graticule was equivalent to 125 μm. Some simple measurements of relative mineral loss were made by comparing, in standardized photographs, the variations in density throughout the dentinal lesions in terms of the density of an adjacent aluminium step-wedge and that of adjacent sound dentine.

Only in a preliminary study were the same specimens microradiographed before and after exposure to the acid gel as it was thought that the dehydration occurring during radiography might alter the susceptibility of the specimen to acid.

Fluoride determinations

In remaining unground sections of crowns and roots a narrow ribbon of dentine weighing less than 1 mg was removed parallel to the cut edge (Figure 1B). One or two sections provided sufficient material for 2 or 3 analyses. Fluoride was measured using the specific ion combination electrode (Orion, model 96-09) after overnight diffusion with 60% w/v perchloric acid at 60°C.

Electron microscopy

Selected specimens were dehydrated in graded alcohols (50%, 70%, 90%, 96%, 2 x100%) infiltrated in a mixture of methacrylates for 24 hr and then polymerized at 60°C for 20 hr. Sections were cut using a diamond knife at 100 nm and viewed on a Philips 400 transmission electron microscope at 100 kV.

Results

Table 1 summarizes the mean fluoride concentrations in dentine samples from teeth from each of several communities differing with respect to the fluoride in the water supply. There were many inconsistencies in the relationship between concentrations of fluoride in water and in dentine. Results of fluoride determinations on serial

sections in several teeth showed a variation of ± 3.5 percent (N=21) around the mean. Many of the teeth from the 1 ppm F area had lower fluoride levels than those from the 0.2 ppm F area and several from the 3.6 ppm F area had lower levels than those from the 2.2 ppm F area.

Because of large differences in fluoride concentrations between teeth from the same community, it was necessary to relate the microradiographic measurements following demineralization to the fluoride concentrations in dentine of individual teeth rather than to groups of teeth from a particular community. Data from single teeth are presented in Tables 2 and 3. In these 2 groups of results, as in 5 others, no clear trend was seen between the progression of the lesions and fluoride levels though there was a tendency for the root dentine sections with the highest fluoride content to show less penetration by the acid. The microradiographic features of some typical demineralized dentine are shown in Figure 2A. In most specimens, a radio-opaque well mineralized band of dentine separated a well defined relatively thick zone of surface demineralization from the narrow demineralizing front of the lesion. As complete demineralization of the outer 50 μm was often present, it was difficult to delineate the position of the original dentine surface. In some of the sections exposed to the more acidified gels (Table 2) it was not possible to detect a radio-opaque intermediate zone.

From microradiographic profiles such as shown in Figure 2B it was possible to calculate the total amount of demineralization. Examples are included in Table 3. Such measurements confirmed the lack of correlation between fluoride concentrations in dentine and the degree of demineralization expressed either as the depth of penetration or the mineral loss.

The profiles of both surface demineralization and the advancing front of the lesion showed more variation along the lengths of the exposed surfaces of sections of crown than of root dentine. This finding reduced the significance which could be attached to the mean figures shown in Tables 2 and 3.

Changes in the extent of demineralization with time of exposure to acid at pH 5.4 are illustrated in Figure 3 for root dentine. Different sections from the same tooth were used for 12 day and 28 day exposure to the same acid gel as it was considered impractical to subject the same sections to a second period of demineralization after being radiographed once. After 12 days, the depth of surface demineralization was very similar in 5 of the 6 teeth and was hardly affected by the fluoride variations. However, there was a negative relationship between the depth attained by the front of these 5 lesions and the fluoride concentration after 12 days, but this was less obvious after 28 days. The slopes representing the rate of penetration of the demineralizing front over the 12-28 day period were similar and were not much affected by variations in fluoride concentrations. Two sections showed evidence of surface remineralization.

Electron microscopy (TEM) of selected sections before and after exposure to acid gels confirmed the microradiographic findings. The suggestion, based on evidence from microradiographs, that root dentine with the highest fluoride levels might show increased resistance to acid (Figure 3 and Table 3) was reinforced by the TEM findings. In the crown dentine from the 0.2 ppm F area it was found that surface demineralization was confined to intertubular dentine, whereas peritubular dentine was also involved at depths of 200-300 μm from the surface.

TABLE 1

Mean fluoride concentrations and standard deviations (ppm) in dentine samples

Source (ppm F in water)	Crown	Root
0.2	249 ± 161 (18)	184 ± 88 (19)
1.0	191 ± 128 (7)	136 ± 85 (7)
2.2	547 ± 372 (13)	596 ± 330 (12)
2.6	535 (2)	610 (2)
3.6	471 ± 420 10)	466 ± 326 (9)
3.8	536 ± 212 (5)	354 ± 102 (7)
5.2	1893 ± 617 (12)	1839 ± 451 (10)

TABLE 2

Demineralization of sections of crown and root dentine produced by exposure to lactic acid 10% gelatine gels, pH 4.6 for 7 days in relation to the fluoride concentrations in drinking water and dentine. Demineralization is expressed in terms of the depth of penetration from the surface (µm).

Source (ppm F in water)	Crown dentine			Root dentine		
	mean ppm F	surface demin.	max. extent of demin.	mean ppm F	surface demin.	max. extent of demin.
0.2	176	65	120	155	95	100
2.6	550	80	145	651	105	145
3.8	660	85	125	472	105	105
5.2	2081	105	105	1681	75	75

TABLE 3

Demineralization of sections of crown and root dentine produced by exposure to lactic acid 10% gelatine gels, pH 5.4 for 28 days in relation to the fluoride concentrations in drinking water and dentine. Demineralization is expressed in terms of the depth of penetration from the surface (µm) and as average percent mineral loss in the outer 400 µm of dentine.

Source (ppm F in water)	Crown dentine				Root dentine			
	mean ppm F	surface demin.	max. extent of demin.	% mineral loss	mean ppm F	surface demin.	max. extent of demin.	% mineral loss
0.2	118	75	200	39	133	137	250	50
1.0	113	95	215	44	85	250	465	64
2.6	80	45	145	31	93	100	215	27
3.8	540	85	235	29	425	215	345	35
5.2	2870	45	185	29	2260	50	125	26

FIGURE 2.

Microradiographs (A ⇒) and mineral density profiles (B ⇓) of two lesions calculated as described in text. Crown dentine from the 0.2 ppm F area (left) and root dentine dentine from the 5.2 ppm F area (right). Bar represents 100 μm. Aluminium step-wedge is shown as is marker of dentine surface.
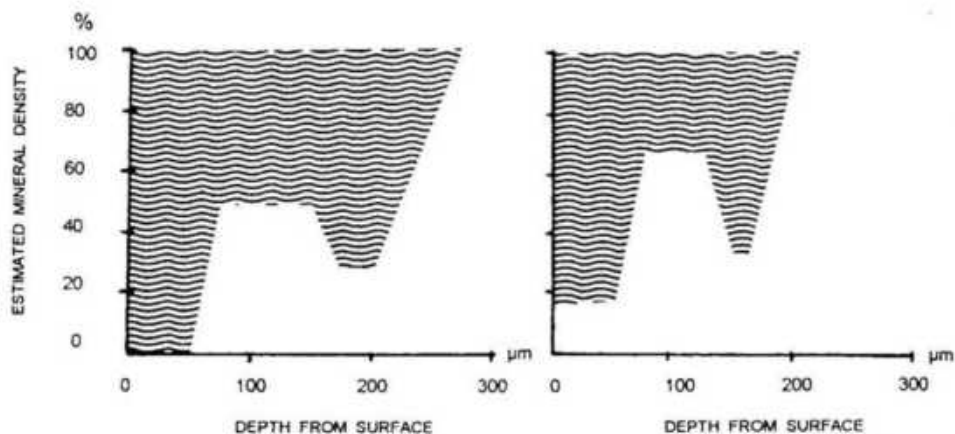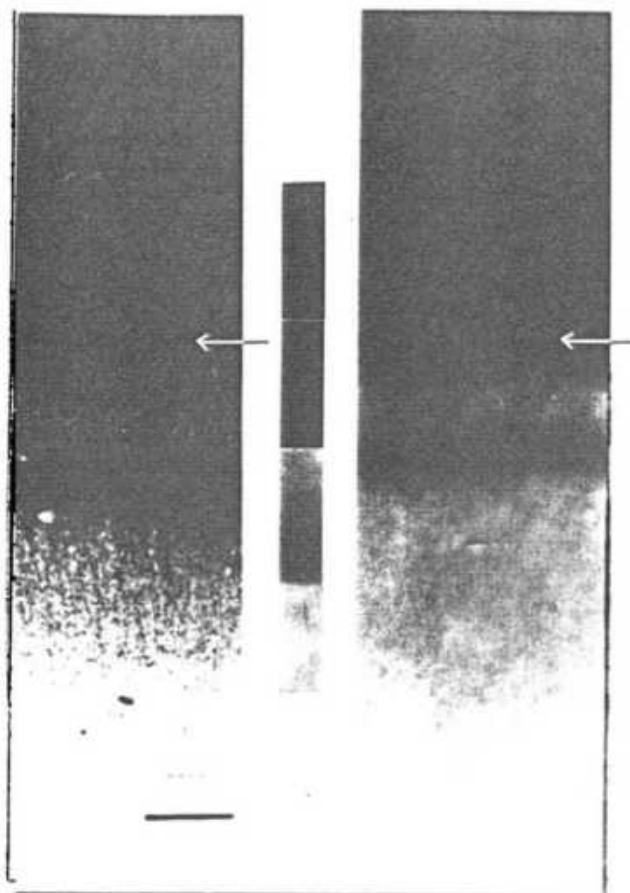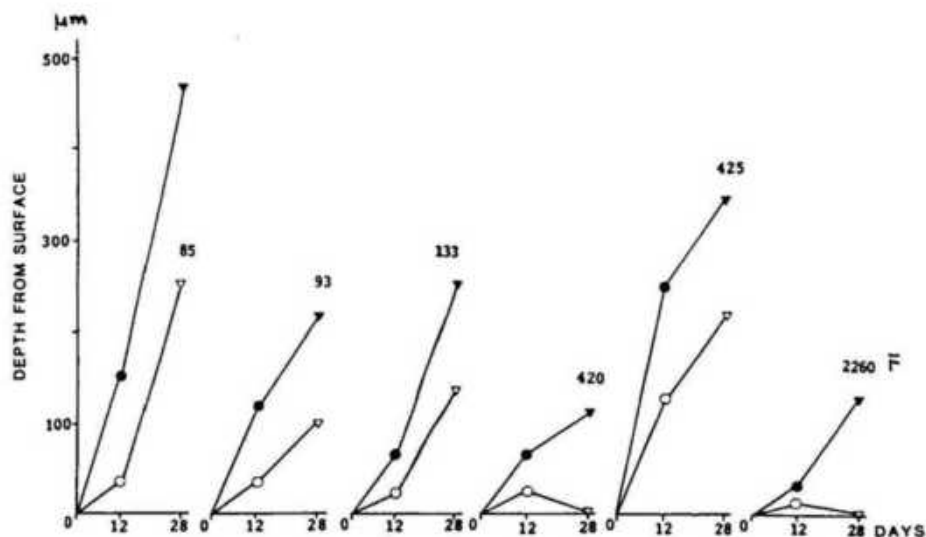
FIGURE 3. Graphical representation of the spread of demineralization in root dentine sections with time in lactic acid 10% gelatine gels at pH 5.4. The solid symbols denote the depth attained by the advancing edge of radiolucency and open symbols the depth of the radiolucent surface zone. The mean fluoride concentration of the dentine samples is shown.

Discussion

The large differences in fluoride concentrations of different teeth from residents of the same community were unexpected. Indeed, some of the results suggested that the recorded history of some teeth was incorrect. Teeth from the 1 ppm F area described as "young, below 20", frequently had lower fluoride levels than those from 0.2 ppm F areas. The age of these teeth could in part account for their lower than predicted fluoride levels as it has been established that age influences the fluoride concentration in dentine and cementum, even in teeth from areas with less than 0.2 ppm F in the water supply (17). Such inconsistencies necessitated that correlations of radiographic data and fluoride concentrations in dentine be restricted to individual teeth rather than to groups of teeth. In addition, they could not be correlated with different geographical sources. The type of correlation carried out was still in keeping with the objectives of the study, namely to relate fluoride concentrations in particular regions of dentine to the rate and extent of demineralization of these regions. However, by studying single teeth the influence which any structural defects within an individual tooth might have on acid-induced demineralization was accentuated.

The variation in fluoride concentrations in both crown and root duplicate dentine samples was larger than could be attributed to experimental error and probably reflected the heterogeneity in fluoride distribution throughout dentine (17).

It must be emphasized that our root samples did not include cementum. Although much higher fluoride levels would have been present if the root surface had been studied rather than a site some one third of the distance between the surface and the root canal (17,18,21), it was considered that cementum might show greater variation in structure and fluoride levels between teeth from the same community than dentine from deeper within the root (8).

Similar considerations applied to the sampling site in coronal dentine. As pulpal dentine contains the highest dental fluoride concentrations (17,19) a site midway between the pulp and the amelodentinal junction was chosen as being more representative of exposure to a particular fluoride level in the water supply.

The microradiographs of demineralized dentinal surfaces in this study were similar in general appearance to those reported by others (8,9,15,22) in that surface and subsurface demineralization were usually produced. Under the conditions of our experiments this surface layer was present as a radiolucent zone of about 50-100 µm in depth in crown dentine. In root dentine its depth was usually greater and more variable than in crown dentine. This observation might be associated with differences in chemical composition of root and crown dentine which have been reported in bovine and rat incisors (23,24).

The demineralization profile showed some variation over the length of the surface exposed to the acidified gels, particularly in crown dentine at pH 4.7. This variation was probably related to greater variation in the direction of the tubules and in the numbers of open and occluded tubules in the crown than in the root samples (13,25). The presence of a radiopaque intermediate zone between this surface demineralization and a diffuse narrow radiolucent front suggested that some remineralization had occured behind the advancing front of the lesion. Extending the time of exposure to acidified gels gave similar increases in the depth of both surface demineralization and the advancing edge of the lesion.

There was a poor correlation between demineralization, based on depth of penetration or estimated total mineral loss, and initial fluoride levels in crown and root dentine. Only the root dentine samples with the highest fluoride concentrations, from residents in a 5.2 ppm F area, showed less demineralization in microradiographs and electron micrographs. An inverse trend between fluoride in root dentine and the depth of the subsurface lesions in one set of samples was not confirmed in others.

Structural differences, some of which are unrelated to fluoride levels, between sections from different teeth, might account for some of our inconsistent microradiographic results. The more variable structure of dentine compared to enamel is partly due to its response to age and trauma (25) and partly to experimental considerations such as dehydration and proteolysis. These factors may override any protective effect of fluoride in dentine against demineralization.

Our failure to find a clear relationship between fluoride in dentine and demineralization is given indirect support by several reports. In one study (11), lesions were produced over 72 hr in roots by acidified gels containing different concentrations of fluoride. It was found that the depth of surface demineralization

and the overall loss of mineral from the lesions were altered only slightly by variations in gel F levels of 1-100 ppm. Concentrations of 550 and 1000 ppm F still allowed severe surface demineralization but less overall mineral loss than lower F levels. Concern that 1.6 ppm F in our undialysed gels might protect dentine from demineralization therefore seems unfounded. It has also been reported that the depths of artificially produced lesions were approximately the same for root surfaces whether or not these were covered by cementum (Feagin, Graves and Clarkson, personal communication). If fluoride were exerting a strong influence on resistance to demineralization, then cementum, with its higher fluoride concentrations, should have afforded greater protection. These two different experimental approaches, in one the dentine containing differing fluoride concentrations and in the other the acid gel having variable fluoride levels, suggested that even high fluoride levels did not prevent demineralization.

There is some disagreement, even in the limited literature, about the relationship between fluoride in dentine and acid solubility. When additional fluoride was incorporated systemically into root incisor dentine of rats, it reduced acid solubility (14). Even so, the fluoride concentration had to be raised from 110 ppm to 3500 ppm to bring about a 25% reduction in the rate of acid dissolution. Topical treatment of dentine with sodium fluoride solutions *in vitro* has been reported to reduce acid dissolution rates (12,13), but similar treatment *in vivo* failed to confirm this (26). In the latter work, fluoride concentrations up to 16,000 ppm were obtained without any reduction in dissolution rate. However, the use of strong perchloric acid to dissolve the dentine may have masked some effect.

It would appear from both experimental work on demineralization of dentine and from epidemiological and clinical findings on root caries (3,27) that any beneficial effects of fluoride depend upon concentrations in excess of those required to reduce enamel caries. The tentative conclusion from the present work supports the view that fluoride incorporated into dentine is unlikely to play a major role in protecting dentine from acid attack.

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FLUORIDES AND THE DECLINE IN
TOOTH DECAY IN NEW ZEALAND

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SUMMARY: National data collected in New Zealand over a 50-year period indicate that the decline in tooth decay in that country commenced before and independently of the introduction of fluoridation and other uses of fluoride. The start in 1977 of a reported steep decline in permanent tooth decay, measured by counting the number of tooth restorations inserted into children's mouths, coincided with a change in diagnostic criteria for provision of such restorations within the School Dental Service, in which 98% of the nation's children are enrolled for treatment. The recent decline in permanent tooth decay has been slightly steeper in nonfluoridated areas. Some professional responses to these data are described and discussed.

Key words: Caries diagnosis; Fluoridation; Fluoride; New Zealand; School Dental Service; Tooth decay.

Introduction

There exists in New Zealand a unique dental epidemiological record. The New Zealand School Dental Service was founded in 1922 and gradually expanded its coverage of the child population until, by 1950, all primary school children up to age 10 or 11 years were able to receive its services. In New Zealand children commence their schooling at age 5 years. By 1965 all school children up to age 12 or 13 years were eligible and 98% of them have availed themselves of the service. After the latter age children leave to attend secondary schools and must then attend private dentists to receive treatment. From the earliest years the School Dental Service kept national records of the dental status of 5-year-olds as they started schooling and, from 1980, of all 12- and 13-year-olds as they left the care of the Service. Unfortunately, with the recent passing of control of the School Dental Service from the Department of Health to various local authorities, reliable national statistics on child dental health are apparently no longer available.

In addition to School Dental Service records, some other child dental surveys have been carried out, though necessarily always among patients of the Service. Less information is available for other age groups of children, though some is available for 8- and 9-year-olds.

The purpose of the present study is to gather together such national information, and information which can reasonably be interpreted as nationally representative, in order to examine the relationship between the decline in tooth decay and the introduction of fluoridation and other uses of fluoride. Also considered are other possible causes of the decline. Hitherto, only the results of small-scale surveys of selected local communities have been presented, purporting to show that the decline in tooth decay, which has undoubtedly occurred over the past 40 or 50 years, was caused by fluoridation.

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Materials and Methods

Data were collected from the following sources.

For 5-year-olds:

1) From 1940 to 1971 the Department of Health, which adminis·ered the School Dental Service, collected information on all 5-year-olds as they enrolled with the Service (1,2). The number of decayed, missing and filled primary teeth ("dmft") and the percentage of such children who were "caries-free" were recorded. This information was for new patients, or random samples of all new patients, not for 5-year-olds previously treated by the Service as preschool patients. As the proportion of preschool patients enrolled gradually increased over the years, from 19% of all preschool children in 1950 to 60% in 1970, the proportion of new patients who were aged 5 years decreased. But the total number of 5-year-olds for whom the information was gathered remained high. In 1988 and 1989 information on all 5-year-olds was collected (2).

2) Health Department information in a Commission report (3).

3) An early study of primary ("deciduous") teeth from 1932 to 1948-50 in the Wellington region (4) where, according to a 1948-50 national survey (5), decay prevalences did not differ from the national average.

4) More recent surveys carried out in 1977 and 1982 (6,7).

5) A retrospective study (8) of school dental clinic patient history charts held by the Department of Health (9). Information was extracted on two patient groups, one born in 1935 (5-year-olds in 1940) and the other in 1955 (5-year-olds in 1960).

For 8- and 9-year-olds:

1) One study provides information for 1980 (10).

2) The WHO study in Canterbury (11,12) reported on this age group for 1973 and 1978. These samples were from a largely nonfluoridated area but have been presented as contributing to the national trend to declining tooth decay (13,14). This was probably justified because in 1976 the "mean number of permanent tooth fillings per child per year" was the same (2.9) for the Canterbury Health District as the national average (15). Also, the recorded 1974-1976 school dental clinic "monthly returns" revealed equal filling rates in non-fluoridated Christchurch (Canterbury) and fluoridated Auckland (16).

3) From randomly selected samples of history charts from the national collection (9), the author obtained the mean DMFT (number of decayed, missing and filled permanent teeth per child) and percentage of children caries-free, for this age group in 1956 and 1959.

4) In Hastings and Napier (the experimental and control cities, respectively, for New Zealand's fluoridation trial) the 1954-55 DMFT and percent caries-free figures for this age group were disparate after almost two years of fluoridation, the younger children's teeth being worse in the newly fluoridated city. It was claimed, belatedly, that the Napier dental statistics differed from the national average because a previously unsuspected soil constituent made children's teeth there more resistant to decay (17-19). However, the published Napier dental statistics for 5-year-olds (19) approximate the later-published national average for 5-year-olds (1), while the Hastings dental statistics for 5-year-olds do not. So the 1955 mean DMFT for Napier 8- and 9-year-olds (18,19) are probably nationally representative. This assessment was confirmed from the national collection of history charts (9).

5) A 1950 WHO-sponsored survey (20), of child tooth decay in New Zealand,

examined 4,072 7- to 16-year-old children in two areas (Auckland and Canterbury Provinces) which contained 52% of the total population at that time.

6) The earliest (1948-1950) national survey of tooth decay in New Zealand (5) used a different index from the "DMFT" one used later. However, its Interim Report (21) shows how that index approximates equivalent DMFT scores. The investigator examined 12,263 12- to 17-year old children in 143 localities and a further 9,359 7- to 11-year-old children in 78 localities. He used X-rays to assist diagnosis. The DMFT equivalents for the 8- and 9-year-olds examined are here presented.

7) The earliest information on this age group, presented as demonstrating a national trend, is provided by the above-mentioned retrospective study (8). The two groups born in 1935 and 1955 were 8- and 9-year-olds in 1943-44 and 1963-64 respectively.

For 12- and 13-year-olds:

1) National statistics for all children this age, as they receive their final treatment with the School Dental Service, were collected from 1980 to 1989, including fluoridation status of their place of residence (1,22).

2) A study using random samples from all School Dental Service patients provides information for 1977 and 1982 (23).

3) The results of the Hastings/Napier 1954-55 dental surveys of older children were reported to represent a national baseline (17,24), being similar in both towns and another, Palmerston North. X-rays were used to assist diagnosis, a fact which could account for the recorded decay levels being so much higher than those found in the 1950 WHO survey.

4) The 1948-50 national survey (5) also used X-rays to assist caries diagnosis for children over age 10 years. Its DMFT equivalent score for 12- and 13-year-olds is accordingly high.

5) The 1950 WHO study (20) provides information for this age group.

6) The Canterbury WHO study (11,12) provided no DMFT figure for this age group. The high DMFT of 10.8 reported for a sample of 13-and 14-year-olds is useless for comparison because 91% of the sample had left school clinics and received fillings from private dentists (12).

7) There were too few history charts for this age group in the national collection to provide a representative sample (9).

Possible causative factors:

1) Information on the introduction of fluoridation to New Zealand communities, and on sales of fluoride toothpastes, is on record (22) and is represented graphically in Figure 1. Widespread fluoridation commenced in 1966. Other uses of fluoride (tablets and clinical applications) commenced around the same time as fluoridation.

2) Until 1977 New Zealand school dental operators diagnosed as "decay" even slight surface defects in permanent teeth. They inserted fillings at that earliest stage of possible decay. Such "thorough" criteria were applied to permanent teeth rather than to primary teeth, and especially to older children receiving their final treatment before passing into the care of private dentists. In 1977 a new filling policy was adopted (25). Instead of "if in doubt, fill" the approach became "if in doubt, wait and see and spend more time on educational and preventive procedures." That was part of a "change to a preventive orientation" described in various studies (11,14,23).

3) Changes in New Zealand dietary habits have been reported (26). Those likely to be relevant to dental health were tabulated.

Results

The data are set out in the Tables and represented graphically in the Figures.

TABLE 1. Decline in tooth decay in New Zealand 5-year-olds (sources in parentheses)

Date of collection	No. of children	dmft	Percent caries-free
1930-32	263 (4)	11.2 (4)	0.76 (4)
1940	505 (2)	8.48 (1)	4.35 (1)
1940	1,039 (8)	8.22 (8)	4.8 (8)
1948-50	692 (4)	7.1 (4)	12.28 (4)
1950	2,057 (2)	6.85 (1)	14.37 (1)
1950	(not published)	7.45 (1)	
1950	13,337 (2)	6.69 (2)	13.5 (2)
1955	(not published)	7.34 (1)	
1955	10,984 (3)	6.6 (3)	14.5 (3)
1960	1,105 (2)	6.07 (1)	16.74 (1)
1960	924 (8)	6.82 (8)	13.7 (8)
1961	9,025 (2)	5.87 (1)	18.9 (2)
1966	1,256 (2)	5.17 (1)	28.03 (2)
1971	1,040 (2)	4.04 (1)	31.08 (2)
1977	998 (6)	3.75 (6)	34 (6)
1982	958 (7)	2.6 (7)	44 (7)
1988	37,808 (2)	2.02 (2)	50.32 (2)
1989	42,864 (2)	2.10 (2)	50.87 (2)

Data for 1930-32 and 1948-50 did not include Maori (around 10% of the population) who at age 5 yr had more decay than children of European descent (5). The two 1955 and last two 1950 entries are from the same survey each year except that Maori were probably excluded for the lower recorded dmft (2). The published data from 1950 to 1960 included permanent teeth (2), but these would be too few at age 5 yr to have much effect on results.

TABLE 2. Decline in tooth decay in New Zealand 8-9-year-olds (sources in parentheses)

Date of collection	No. of children	DMFT	Percent caries-free
1943-44 (8)	1,039	4.3	2.2
1948-50 (4,5)	957	4.1*	
1950 (20)	1,049	3.5	7.1
1955 (18)	395	3.5	
1956 (9)	336	3.5	10
1959 (9)	404	3.4	10
1963-64 (8)	924	3.9	10.35
1973 (11)	557	3.3	11
1978 (11)	529	2.0	31
1980 (10)	978	1.3	46

* Diagnostic X-rays used

TABLE 3. Decline in tooth decay in New Zealand 12-13-year-olds (sources in parentheses)

Date of collection (source)	No. of children	DMFT	Percent caries-free
1948-50 (4,5)	3,796	12.7*	
1950 (20)	1,003	8.0	0 6
1954-55 (17,24)	550	10.7*	
1977 (23)	961	7.1	2.4
1980 (22)	58,095	5.1	7.1
1981 (22)	58,962	4.5	9.1
1882 early (23)	1,042	3.7	13.4
1982 later (22)	59,151	4.1	11.8
1983 (22)	59,039	3.8	15.6
1984 (22)	61,255	3.4	18.7
1985 (22)	58,301	3.2	20.4
1986 (22)	56,757	3.0	23.5
1987 (22)	52,531	2.8	24.9
1988 (22)	50,782	2.5	28.4
1989 (22)	51,355	2.2	31.9

* Diagnostic X-rays used

TABLE 4. Decline in tooth decay in New Zealand 12-13-year-olds
in combined fluoridated and combined nonfluoridated areas (2)

	All fluoridated areas (higher av. income)*			All nonfluoridated areas (lower av. income)*		
	No. of children	DMFT	Prevalence (100 - % caries-free)	No. of children	DMFT	Prevalence (100 - % caries-free)
1980	31,093	4.6	92%	26,998	5.6	94%
1989	25,921	2.1	67%	25,434	2.4	69%
% decline		54%	25%		57%	25%

* The two kinds of area differ socio-economically (30,31)

TABLE 5. New Zealand's changing diet: consumption per head of population per year (kg)

Sugar   1930: 42   1940: 50   1950: 51   1960: 42   1970: 51   1980: 53   1984: 48

Fruit   1930: 28   1938: 52   1948: 48   1957-8: 48   1969: 52   1972: 65   1976: 69   1981: 80

Vegetables   Prewar to 1950s: 32   1963: 58   1969: 101   1972: 85   1976: 83   1981: 100

Cheese   1930: 2   1938: 2   1944: 3   1950: 3   1960: 3   1970: 4   1978-79: 8   1982-83: 8

Figures are to nearest kilogram. Vegetables exclude potatoes, which remained at around 40-50 kg. Other changes were: increases in Vitamin C and other micronutrients due to increases in fresh fruit and vegetables, household refrigeration, and changed methods of cooking (26).

FIGURE 1 (upper). 50-year decline in tooth decay of 5-year-olds
Solid line: mean number of decayed, missing or filled teeth (dmft)
Broken line: Tooth decay prevalence (100 - % decay-free)
Fluoridation (solid line): Percent of population with fluoridated water
Fluoride toothpaste (broken line): Percent of total toothpaste sales

FIGURE 2 (lower). Declines in tooth decay (mean dmft or DMFT)
for children aged 12-13, 8-9 and 5 years.
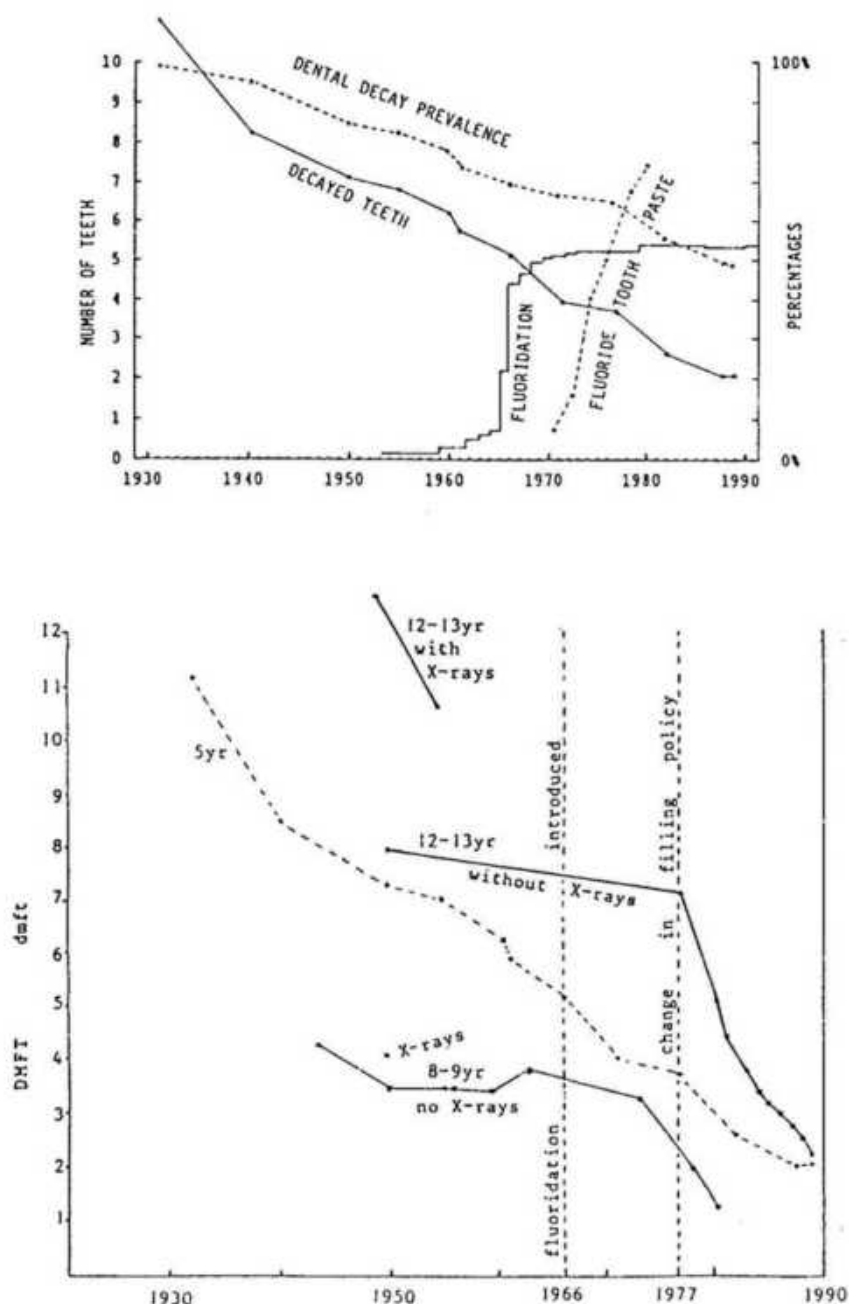
Discussion

The decline in tooth decay of primary teeth clearly commenced before the introduction of fluoridation and other uses of fluoride (Table 1 and Figure 1), which could have only accelerated a decline already under way. While the decline has been justifiably described as a "mystery" (27), it correlates well with the changes in diet which occurred (Table 5). Sugar consumption has remained high, but consumption of fresh fruit and vegetables, which contain important micronutrients, and cheese, known to be decay-inhibiting (28,29), has increased. Those changes could account at least in part for the increased immunity to the disease, now enjoyed by over a quarter of the older children in both fluoridated and nonfluoridated areas (Table 4).

The areas compared in Table 4 are dissimilar socio-economically and in other ways (30,31). Greater differences in decay prevalence existed between such dissimilar areas before fluoridation was introduced, lower income areas having more decay (32). Today, when similar socio-economic areas are compared, decay prevalence is slightly less in nonfluoridated areas (30,31). Table 4 also shows that dental decay has declined slightly more in the nonfluoridated areas of New Zealand. It is now well-established by several studies that teeth formed in fluoridated areas are damaged by the fluoride (33). Might not such fluorosed teeth also be more prone, ultimately, to tooth decay? The decline in fluoridated areas since 1980 could not have been caused by the 1966 introduction of fluoridation, because all the children compared had received lifelong exposure to fluoridated water.

The overall decline in permanent tooth decay is similar to that for primary teeth (Tables 2 and 3, and Figure 2), but the pattern of the decline is complicated by the sudden reduction of fillings in permanent teeth, reflected in an immediate very steep decline in DMFT and decay prevalence, following the 1977 change in diagnostic procedure. It was acknowledged that such a reduction was too steep to be wholly a reduction in tooth decay prevalence (23). Surveys have revealed no increase in the "D" (decayed) component of DMFT scores compared with earlier surveys (11,14,23). Those facts suggest that, for some years before 1977, permanent teeth in New Zealand were being "overfilled" - that is, filled rather more often than was really necessary. Many private dentists continued such overfilling after 1977 (34).

Clearly, a reduction in recorded DMFT scores does not necessarily reflect a reduction in tooth decay. Historical research has shown that the reductions in DMFT reported following the Hastings, New Zealand, fluoridation trial were partly if not mainly the result of unpublicized changes in diagnostic criteria, in Hastings school dental clinics only, after the trial commenced (35-37).

The use of X-rays by some early examiners does complicate interpretation, because such use increased greatly the "D" component of early DMFT scores. There appears to have been a decline in X-ray-measured DMFT between 1948-50 and 1954-55. X-rays revealed smooth surface decay between teeth which was often undetectable without X-rays. Today in New Zealand, following a great decline in the prevalence of such smooth-surface decay, the use of X-rays has been shown to make much less difference to the detection of decay in permanent teeth (38,39). So for 12- and 13-year-olds the decline (Figure 2) from the early radiographically measured levels to today's levels could indicate the actual decay decline. But, even when the "with X-rays" results are disregarded, the overall declines from 1950 to today are similar for permanent and primary teeth.

It has been argued that an early School Dental Service practice of "prophylactic odontotomy" (a kind of "preventive" filling in vogue from the late 1930s to early 1950s) could have inflated early DMFT scores. However, in 1957 Dr Bruce Bibby, Director of the Service, reported that such fillings accounted for only one in every 500 placed (40).

The data presented in the present study have been questioned because of differing diagnostic standards of the early examiners. The New Zealand examiners in 1948-50 and 1954 and the American one in 1950 probably did have different concepts of what was "decay". (The same argument can be applied, of course, to the various studies cited below by the Health Department.) However, New Zealand children have had a high proportion of their DMF teeth in the "F" category, and little variation occurs between examiners in the counting of filled teeth. Changed diagnostic standards of operators, rather than of examiners, caused the big declines in DMFT and apparent decay prevalence.

The New Zealand Department of Health, when first faced with the above evidence on 5-year-olds, agreed that the decline in primary tooth decay had started well before the use of fluorides, but stated that the recent decline in both primary and permanent tooth decay "is believed to be related to the increased availability of fluorides in tablet form and, in particular, in toothpaste, and fluoridation, and a change to a preventive orientation in the School Dental Service" (41). Two sets of statistics were presented to support that belief, still held by the Department and most members of the dental and medical professions.

The first set had been published earlier, in graphic form (14). It consisted of mean numbers of fillings placed per child per year in the School Dental Service, at 5-yearly intervals, to indicate that the decline in permanent tooth decay did not start until after fluoridation had been widely implemented in 1966:

Year	Fillings per child
1955	5.1
1960	5.2
1965	5.0
1970	4.4
1975	3.5
1980	1.5

The above figures are for dissimilar child populations, of differing average age and distribution of ages. After 1950 all schoolchildren received regular free dental treatment from either the School Dental Service or from private dentists at state expense. The above figures are for only School Dental Service patients. But because of a post-war "baby boom" the School Dental Service had to release older schoolchildren, some as young as 8 years old, to private contracting dentists for treatment, which is not included in the above set of figures. In 1955 only 59% of primary schoolchildren (up to 10 or 11 years old) could be treated at school clinics. After that year, as the Service again expanded its coverage of the child population, it gradually brought the older age groups under treatment again (1,42). So the above figures for 1955 and 1960 are for younger children than are the figures for 1965 and 1970.

Younger age groups have lower filling requirements, simply because they have fewer teeth. If the fillings for the older children had been included, the above 1955 and 1960 figures would have been much higher. The figures as presented thus mask any decline occurring during the earlier period. That is, the decline probably extended over the whole of the above period 1955-1980, instead of, as the figures imply, commencing after 1966 when fluoridation became widespread.

The second set of statistics (41) consisted of mean DMFT from various studies, for two age groups. Its "12 and 13 year olds" column has since been published (43). This set was also claimed to show the effect of fluoridation after 1966:

Year	Region	DMFT (8 & 9 year olds)	DMFT (12 & 13 year olds)
1948	Wellington Province	4.4	9.4 (11-12 yrs)
1950	Auckland & Canterbury Provinces	3.5	7.9
1954	Hastings	4.2	10.7*
1958	Palmerston North	4.2	10.4*
1959	Lower Hutt	4.5	10.0
1962	Owaka	4.5	9.8* (12 yr only)
1966	Seven soil areas	3.7-5.2	9.4-12.0
1973	Canterbury	3.2	10.8 (13-14 yrs)
1977	National		7.0
1980	National	1.4	
1982	National		3.7

* Radiographs used

The department stated of the above set: "The decline in dental caries of permanent teeth commenced between 1966 and 1973..." Yet the first post-fluoridation figure, for 1973, is from Canterbury, a nonfluoridated region. Some of the above figures are not national ones, being from various local studies. The "seven soil areas" (44) and Owaka (45), were small rural communities hardly comparable with the city populations and certainly not nationally representative. Their sample sizes - not shown in the above set (41), nor in the published version (43) - were small. The Owaka 12-year-olds sample contained twelve children.

The pitfalls are many when trying to deduce tooth decay prevalence changes from past recorded data. However, while the New Zealand data on permanent tooth decay are consistent with various interpretations, it seems probable that, because the decay process is essentially the same for both primary and permanent teeth, a real decline in permanent tooth decay as well as primary tooth decay occurred in the earlier years, independently of fluoridation and fluorides.

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SCIENTIFIC KNOWLEDGE IN CONTROVERSY
THE SOCIAL DYNAMICS OF THE FLUORIDATION DEBATE

Brian Martin

Reviewed by Frederick I Scott Jr *

Brian Martin has written a remarkably comprehensive account of the history and dynamics of the controversy surrounding the addition of fluoride-containing salts (artificial fluoridation) to community drinking water for uncontrolled consumption by the public *(Scientific Knowledge in Controversy: The Social Dynamics of the Fluoridation Debate.* State University of New York Press, Albany NY 1991). It should be required and desired reading for anyone interested in science and scientific research, particularly in regard to public policy, and for educators seeking insights toward the goal of achieving science literacy among scientists-to-be and nonscientists-to-be.

Almost maddeningly scrupulous in maintaining neutrality by refusing to comment on the material he reports, Martin brings valuable insights even to some longtime followers of the controversy. Nevertheless, he leaves unexamined two aspects that, in my opinion, go not only to the heart of the controversy but to the role and responsibilities of social science research to enlighten the public. A look at Martin's approach provides the foundation for addressing the questions raised. He sets out to analyze the fluoridation controversy "as a power picture of science," as a social component of society, and as a social activity in its internal operation. To do so, he approaches it "at a series of different levels" to show "the exercise of power on a successively larger scale."

He "examine[s] the arguments raised by scientists who support or oppose fluoridation in relation to benefits, risks, individual rights, and decision making" before probing the "remarkable coherency of viewpoints" which characterize the proponents and opponents of fluoridation. After exploring the struggle for credibility between the two sides, he moves to examine the overt use of the power of the dental profession against antifluoridationists and the role of industrial corporations whose interests may have shaped the context of the debate.

With this setting, Martin attempts to draw out some implications of the analysis, to suggest *how* the debate should be resolved, if, indeed, it *can* be resolved, finally concluding that there is no simple answer to these questions. His closing chapter deals with the social analysis of the fluoridation controversy, describing standard approaches in previous studies as contrasted with his own, and the difficulty for the researcher of contemporary controversies to avoid direct involvement in the controversy.

Despite the thoroughness of his analysis of the fluoridation controversy, Martin disclaims concern with supporting or opposing fluoridation. His "interest lies in the

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exercise of power within science and the implications of this for democratic decision making" in the belief that the method of analysis he has chosen helps in dealing with these issues (p106). That studied attempt for neutrality apparently leaves him as unsatisfied as Edward Groth III, for he concludes the book with Groth's 23-page commentary, "The Fluoridation Controversy: Which Side is Science On?" (A 25-page appendix on the status of fluoridation around the world completes the text of the book).

Edward Groth III is a biologist who has specialized in the study of policy decision-making processes on environmental and public health issues. He holds an AB degree in biology and a PhD in biological sciences and has prepared reports on environmental problems as a former staff member of the National Research Council in Washington DC. Currently he is technical director for Policy and Public Service of Consumers Union, publisher of *Consumer Reports*. Groth finds Martin's assessment unsatisfying for its failure to say more about two key questions.

First, Martin takes the existence of the controversy over fluoridation as a given without examining *why* the controversy persists. Second, while Martin recounts what both sides of the dispute say, he makes no attempt to assess the evidence presented by the two sides, offering no guidance as to which side, if either, may be right. Groth's essay attempts to fill those two voids to demonstrate "that the controversy over fluoridation is, indeed, inherent in the proposal and absolutely unavoidable" and to provide his assessment of the quality of the evidence.

Although Groth notes that substantial scientific critiques of the fluoridation studies have never been effectively shown to be in error, he concludes that the overall quality of the evidence on the health aspect differs little from that of other environmental health issues with both good studies and bad studies. He reports without comment on the 1989 change in claimed benefit from 50-60 percent reduction in tooth decay to a much disputed claim of up to 25 percent reduction. Nor does he comment on the failure of proponents to address the parallel and comparable reduction in tooth decay that has occurred in nonfluoridated communities. He does believe that "a great number of animal experiments, clinical trials, and other studies ... provides almost indisputable evidence that fluoride is an effective anti-caries agent." He does not comment on the evidence that fluoridation temporarily delays the decay process by approximately two years so that by about age 19 the decay rates are identical for fluoridated populations as compared to non-fluoridated populations (1-3). He sees "a great deal of evidence of potential risk but little conclusive proof of harm; and nothing like conclusive proof of safety for various populations using water with 1 ppm fluoride over a lifetime."

Thus, Groth concludes that science is on neither side and that objective scientific inquiry is unlikely to affect public policy debates over fluoridation.

Despite their extensive and intensive analyses of an exhausting array of material, both Martin and Groth leave me exasperated and more thoroughly disappointed in the perceptions of science held by scientists. While both researchers touch on what I see as the key elements in the matter, neither expressly poses the questions nor suggests ways of proceeding toward resolution. Their highly commendable efforts seem largely to indict the practice of science, both physical science and social science.

First, I take science to be a process, a formalized way of proceeding to acquire information of appropriate certainty about functional relationships. The key word is *process*, an ongoing system of operations leading to the discovery of relationships

within some framework. True, not much of what passes for science today meets those criteria, but they serve as gauge and goal.

In the case of fluoridation of public water supplies, science can be brought to bear on the question of efficacy - does the presence of fluoride ion in drinking water reduce the incidence of dental caries in those who drink it? Under what circumstances? Does it cause harm?

While there are undoubtedly differences in what individuals define as science, I do not believe that any definition of science includes the determination or advocacy of public policy though, of course, individual scientists may feel compelled to argue for or against courses of action based on their understanding of the findings of the scientific process. In their roles as social scientist observers and commenters on "scientific knowledge in controversy," Martin and Groth correctly decline to take stands on the scientifc evidence in the matter of fluoridation. They commit a fundamental error, however, when they fail to comment on the way in which science has been practiced in the matter under consideration. True, a critical commentary by social scientists on the practices of physical scientists would invite the turnabout that should be an integral part of the feedback process essential to the responsible practice of science. At the very least, however, social scientists seeking to enlighten the public on a scientific controversy should examine how science might proceed *from this point* to develop additional information useful in the determination of public policy.

This failure touches the heart of the concern for "scientific literacy" in the general public. If dedicated social science researchers, after intensive study of the scientific literature and the social dynamics of a long-term difference of scientific opinion, do not even acknowledge a responsibility to discuss ways the public can ask the physical and biochemical science researchers to develop information needed to make or monitor public policy, the public has a *prima facie* case that "science" doesn't give a tinker's dam about its much-touted dedication to the public good.

Second, I believe the prime responsibility of persons serving in scientific positions in the public health service is to seek to discover and report faithfully on scientific relationships pertinent to the making of public policy. They can advocate for or against policy based on the information at hand, but the appropriate discharge of that responsibility requires that they propose and undertake research seeking additional information necessary to resolve significant uncertainties related to the determination of public policy.

Martin and Groth make no mention of that responsibility of public health scientists. I take that also to be a failing of social science seeking to examine the social dynamics of a scientific controversy. From the material presented in the book, several specific recommendations and observations related to these two points could have been made without recourse to more recent findings.

For example, there are several points of agreement in the scientific evidence presented by the proponents and opponets of fluoridation:

1. Dental fluorosis occurs at a fluoride concentration in water very close to that recommended for the prevention of dental caries, which is considered to vary with the average annual temperature (p182). Controlling the *concentration* of fluoride in water does not determine the *total amount* of fluoride ingested which varies, of course, by the total amount of water (and water containing foods) one takes in, a figure that varies widely.

2.   The current understanding of the effect of dental fluorosis (p182) is inadequate in terms of both toxicological and psychological effects on children. Indications that it is increasing have triggered debate but no major effort to resolve it for some 20 years (p183).

3..   Virtually none of the studies on which support for fluoridation is based had adequate control for factors other than fluoridated water that might affect tooth decay rates (p180) or toxicity, despite strong evidence that some effects in sensitive people may be very likely (p186).

The much-touted scientific method purports to test an hypothesis against experimental evidence and to refine the hypothesis for further experimental verification. Given these agreed-upon uncertainties, Martin and Groth would be fully justified in recommending more carefully planned and conducted research. Colquhoun (4,5) has already shown a connection between socioeconomic (mainly income) status and dental health as measured by freedom from dental caries and lowered filling rates that could serve as a basis for such research. Colquhoun's credentials are unassailable. With over 35 years experience as a dentist and dental researcher and administrator, he has dealt with fluoridation as a professional person favorably inclined to the practice and as researcher examining the practice in significant detail.

Martin closes with an extensive analysis of social analysis ("Studying the Controversy," Chapter 8, pp148-168) that enlightens me as to the concerns and processes of "sociologists and political scientists" (p148) and dismays me that those concerns and processes should serve so well to obscure the analysis it professes to seek. Granted that many social analysts seek to "'contribute to social science,' as well as to enhance their own reputations and promote their careers" (p167), the primary purpose for the expenditure of energy and funds on the task must be the discovery of elements deemed vital to the understanding and possible resolution of the controversy.

Without that objective, the effort is a waste for the community supporting it. Certainly, in the course of the study, one need not be expected to avoid making a personal judgement about the information obtained. The value to be gained by the community rests in the guidance provided by the process of acquiring the information, by the comprehensiveness of the information obtained, and by the criteria applied to the quality of the process by which the controversy has been managed.

By these criteria, Martin informs us well regarding his process of gathering the information. He succeeds admirably in the comprehensiveness of the information gathered. His failure to examine explicitly the quality of the controversy's management, however, piques a new level of frustration with the fluoridation controversy. Groth responds, in part, to this pique in his examination as to whether or not the controversy is a genuine one and in his examination of the dispute over scientific issues. He, too, fails to extend the analysis in important aspects as noted above.

Martin recounts (pp82-86) the tactics used by proponents of fluoridation to discredit the personal reputation of those who have raised serious scientific objections to the practice while completely failing to respond to those objections. He further reports (p165) his difficulties in getting comments (receiving only four responses of 12 sought) from proponents on the draft of this book. These inclusions do provide some guidance to the reader as to the quality with which the process has been managed though explicit observations are not made, leaving both the scientific and the lay reader with no guidance as to questions, if any, to be resolved or the value to be obtained by their resolution.

Thus, Martin's remarkable treatise brings useful analytical insights, particularly when contrasted with his report of the approach taken in other social analyses of fluoridation, but leaves much to be desired in enlightening the scientific and lay public regarding the possibility of progress in the fluoridation controversy. The failure to point out the responsibility of public officials and publicly funded researchers to examine and resolve satisfactorily agreed-upon questions of likely harmful effects irrespective of any anticipated benefits indicts both social analysis and biomedical science research.

Recent reports of such harmful effects correlating water fluoridation and hip fracture among the elderly in the United States (6,7) and in England (8) and increased osteosarcoma rates among young males in New Jersey (9) attest the significance of failure to pursue questions raised four decades ago. Even those disturbing revelations, however, are unlikely to redress a pervasive absence of integrity in the administration of science.

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The following are abstracts of papers presented to the XIXth Conference of the International Society for Fluoride Research, at Kyoto, Japan, September 1992, in the sessions on *Effect of Fluoride on Humans*, and on *Biological Effects of Fluoride*.

EFFECTS OF FLUORIDE EXPOSURE ON THE HEALTH OF WORKERS IN AN ALUMINIUM SMELTER

G F Sun[1] and Y L Hu[2]

Fluoride exposure is a major industrial hazard in aluminium smelting. To evaluate long-term health effects of F exposure, 185 exposed workers in electrolysis and cryolite production workshops and 150 non-exposed F workers in the same district were selected for study. The results were:

1)   The average HF concentration in the air of the workshops during the past 20 years was 4.95 mg/m^3 and in dust 42.13 mg/m^3, which were 3 and 9 times the MAC (maximum allowable concentration), respectively.

2)   The prevalence of neurasthenic syndrome, skeleton and muscle pain syndromes and gastrointestinal disturbance in F exposed workers was significantly higher than in the controls. The prevalence in cryolite workers was higher than in electrolysis workers.

3)   EKG test showed that the rate of sinus arrhythmia, left ventricular high voltage, and sinus bradycardia were significantly increased.

4)   Bone changes were revealed in most F exposed workers by X-radiography. Among them, pelvis bone density increase was 26.5%, density decrease 4.3%, "gauze form" of bone strucure 12.4%, and "ground-glass-like" 12.4%. The ossification in obturator membrane, bone node ligament, coxa-lumbus ligament, ulna-radius interosseous membrane and tibia-fibula bone membrane was 42.9%, 38.2%, 23.5%, 21.2% and 41.2%, respectively. Ossification of the hip joint, knee and elbow was 22.9%, 31.2% and 6.4%, respectively. Lumbar vertebrae change was 75% and sternum change 28%. The changes were related to the length of service with F exposure.

5)   The bone cortex index was markedly increased in F exposure workers, especially for the tibia diaphysis, epiphysis and ulna-radius diaphysis. The increase was also related to F exposure.

6)   Laboratory tests showed that the level of F in the hair of F-exposed workers was significantly higher than that of both control and other workers in the F-contaminated district. For workers dropping out of F exposure the level markedly decreased. Although urine F concentration in F-exposed workers increased, no relationship with the conditions of F poisoning was found except for the positive correlation with hair F level. The data showed that the effects of F on the health in the Al smelter were serious and more attention should be paid to them.

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STUDY OF THE EFFECT ON PULMONARY FUNCTION IN WORKERS WITH CHRONIC EXPOSURE TO ORGANIC FLUORIDE

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Inhalation of elevated concentrations of organic fluoride can cause acute pulmonary function damage and also lead to lung fibrosis. To evaluate pulmonary function in chronic organic F exposure, 163 organic F exposed workers in Fuxin Fluoride Chemistry Factory were selected for study, and the non-exposed F workers in the same factory were the controls. Pulmonary function test was done with an FJD-80 spirometer. The predictive value below 80% for FVC, FEV1.0, FVC1.0/FVC and below 70% for FEV25-75%, FEV75-85%, V75, V50, V25 were classified as abnormal. The results were:

1) The abnormality rate in organic-F exposed workers was significantly higher than in the controls, especially for FEV1.0. Thus long-term chronic F exposure can cause ventilation disturbance mainly in the middle air passage.

2) Among the organic F exposed group, the abnormality rate in male workers was markedly higher than in female workers, but the condition was not seen in the controls. Further analysis showed that the results were related to smoking. In the control group, there were no differences in pulmonary function abnormality between male and female smokers, but in the study group the damage in smokers became outstanding, thus illustrating that both smoking and organic F exposure could have a synergistic damaging effect on pulmonary function.

3) The level of pulmonary function damage was related to different types of work in the study group. In the polymerization and solution workshops, the damage to workers was more serious than in other workshops. The organic F contamination and the properties of the products in the workshops may be the main causes.

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BONE MINERAL DENSITY IN INHABITANTS OF AN ENDEMIC FLUOROSIS AREA

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Recently, many techniques for measuring bone mineral density (BMD) have been developed. Of these, dual energy X-ray absorptiometry (DEXA) has been reported to be the most sensitive, precise and accurate method for detecting bone mineral loss and has become relatively common in the diagnosis of patients with osteoporosis. Increases of bone density in X-ray pictures have been reported as the main skeletal change in osteofluorosis as contrasted with osteoporosis. However, assessment of skeletal change from X-ray results is often difficult, especially in early stages of osteofluorosis commonly encountered. We examined bone mineral density of the spine (L1-L4 BMD) in subjects in an endemic area using DEXA. Among 17 subjects who had drunk high levels (2.40~5.25 ppm) of fluoride in water for a long time, no case of definite osteofluorosis was observed. A few of the F-exposed subjects showed high L1-L4 BMD values compared with controls.

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PANCREATIC BETA-CELL FUNCTION IN ENDEMIC FLUOROSIS

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Chronic fluoride toxicity occurring as a result of consumption of fluoride polluted drinking water continues to be a widely prevalent disorder in India. With the recognition that fluoride has a direct effect on the cellular C-GMP system, attention has shifted to the non-skeletal effects of excess fluoride. Based on preliminary evidence in the literature that fluoride may alter insulin secretion from the rat pancreas, we studied 25 subjects in the age range of 10 to 30 years with frank skeletal fluorosis from District Unnao in the state of Uttar Pradesh. A similar number of age, sex and weight matched controls from non-endemic areas were also studied. Venous samples were drawn in the fasting state and at 1 and 2 hours following a 75-gram glucose load. Plasma glucose and insulin estimations were carried out on all the samples, - 25-OH-vitamin D and $1,25-(OH)^2$ vitamin D levels were estimated in the basal sample.

Although basal glucose level was normal, abnormal glucose tolerance was found in as many as 10 out of these 25 patients (Group A) as compared with fluorosis patients with normal glucose tolerance (Group B) and non-fluorotic controls (Group C) (A vs B: 0 hr $p<0.01$, 1 and 2 hr $p<0.05$; A vs C: 0, 1 and 2 hr $p<0.05$). Also, 3 out of these 10 patients had peak insulin levels over 200 microunits per ml. Groups B and C had comparable glucose-insulin profiles. There was no correlation of these abnormalities with vitamin D levels. The village was meanwhile provided with low fluoride water supply. Most interestingly, on testing 6 months later, there was a complete reversal of these abnormalities, with normalisation of the glucose-insulin profiles. Our study suggests the presence of abnormalities in pancreatic beta-cell function and glucose tolerance in endemic fluorosis, which may be reversible on removal of the fluoride insult.

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AN EXPERIMENTAL STUDY ON RENAL EXCRETION OF FLUORIDE

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In our preceding studies with rats with glomerulonephritis, both the nephritic condition and supplemental fluoride drinking water had an effect on the fluoride content of calcified tissue, bone and teeth. The histological features of nephritis were not enhanced by fluoridation in rats.

In human patients with renal dysfunction, the higher the creatinin value, the higher becomes the non-ionic fluorine in clots or in whole blood. A single hemo-dialysis procedure in patients eliminates as much as 8 ng F/ml from serum.

The relationship of fluoride metabolism and kidney function should therefore be a theme of medicobiological studies.

The renal artery was irrigated by fluorinated blood or fluoride solution in experimental dogs. Ureter and venal samples were analyzed to examine the level of fluoride metabolism in normal kidney.

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STUDIES ON THE MECHANISM OF FLUORIDE TOXICITY TO RENAL ENZYMES AND ANTAGONISM OF BORON TO FLUORIDE

J Li, R Chen, M Zhang and G Zhang

The mechanism of toxicity of fluoride to renal enzymes and the mechanism of antagonism of boron to fluoride were studied by means of enzymatic biochemistry, histochemistry, cell culture, radioactive isotope trace techniques, ultrastructural pathology, microelemental analyses, ultraviolet spectroscopy (UV), fluorescence, circular dichroism (CD), infrared (IR), ^{1}H and ^{19}F nuclear magnetic resonance (NMR), quantum biophysics at the various levels of quantum, molecule, subcell, cell, organ, experimental animal and human body, *etc*. The results of the studies were as follows:

1) Fluoride inhibited the activities of renal succinic dehydrogenase (SDH), acid phosphatase (ACP) and alkaline phosphatase (AKP), and increased the excretion of urinary r-glutamyltransferase (r-GT). The inhibition of fluoride toward renal AKP belonged to the competitive inhibition.

2) Fluoride damaged the organelles related to protein synthesis in renal tubular cells, interfered with anabolism of proteins in renal mitochondria and microsomes, and reduced the content of copper and zinc in renal cytoplasm, so that the quantity of renal enzymes was decreased.

3) Fluoride conjugated the phenolic hydroxyl of tyrosine by hydrogen bonding and destroyed the normal spatial conformations of proteins, so that the quality of real enzymes was changed.

4) Boron combined with fluoride in the body to form tetrafluoroborate (BF_4^-), which was excreted in urine, and decreased the permeability of fluoride through cellular membranes. Both effects of boron reduced the content of fluoride in renal cells, so that the toxicity of fluoride to renal enzymes was antagonized by boron.

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DISTRIBUTION PROFILES OF FLUORIDE IN THREE DIFFERENT KINDS OF RAT BONE

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This study was performed to determine the distribution profiles of fluoride in the three different kinds of rat bones: humerus, vertebra and temperoparieta. Histological observations were also used to explore reasons for and biological meanings of this distribution. Two groups of Wistar rats were administered water containing 0 and 100 ppm of fluoride, respectively, for 24 weeks. The fluoride distribution profiles in the whole layer, from the periosteum to the endosteum, of the three different bones were determined by means of the abrasive microsampling technique. In the controls the profiles in humerus, vertebra and temperoparieta looked like the shape of a "U", "W" and "U", respectively. In the experimental group, however, the three profiles changed to the shape of a "/", "W" and "V". The differences of the fluoride distribution profiles were explained by the histological appearances of these bones, and some relationships between the fluoride distribution and the histological structure of bone were also considered.

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EFFECTS OF FLUORIDE ON IMMUNE SYSTEM FUNCTION

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The fluoridation of public water supplies was introduced over 40 years ago in the belief that it was beneficial to teeth. More recent evidence, however, reveals no lasting benefit and suggests that fluoride may be harmful to many physiological systems. The present study investigates effects of fluoride on the immune system. The results show that concentrations of 0.5, 1.0, 2.0 and 20.0 μg/ml significantly inhibit the ability of white blood cells (leucocytes) to migrate after incubation for 3 hours at 37°C. The concentrations include those used in public water supplies and the ability of leucocytes to migrate was significantly impaired even at the lowest concentrations. All the concentrations are lower than those used in fluoridated toothpastes, topical gels and mouth rinses, which are often swallowed, particularly by young children. In this study the white blood cells were exposed to the various concentrations for 3 hours. Where water fluoridation is undertaken, exposures are continuous and life-long, reported values for plasma fluoride ranging from 0.7 to 2.4 μg/ml. While some of the blood samples used in this study showed little or no inhibition at those low concentrations, some were obviously affected, the mean effect being significant at all concentrations. The author concludes: "A section of the population may therefore be at risk of compromised immune system function from water fluoridation schemes. All recent large-scale surveys have shown minimal benefits to teeth from fluoridation programmes. On the other hand, chronic exposure to fluoride at 1μg/ml could have a long-term detrimental effect on the general health of the population. Over the past 20 to 30 years there has been a substantial and unexplained rise in a number of conditions such as allergy, auto-immune diseases and the post viral fatigue syndrome. The common factor in these conditions is an alteration in the efficiency of the immune system."

CANCER INCIDENCE AND MORTALITY IN WORKERS EXPOSED TO FLUORIDE

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Background: Although a recent bioassay showed increased frequency of bone cancer in rats with high oral intake of fluoride, the data are reported as equivocal evidence of carcinogenicity. In humans, occupational fluoride exposure may cause skeletal fluorosis, and our earlier follow-up of fluoride-exposed workers showed increased incidence of respiratory cancers.

Purpose: To further evaluate occupational fluoride exposure as a carcinogenic risk factor, we extended by approximately one decade the follow-up of a cohort of 425 men and 97 women employed for at least 6 months in the period 1924-1961 at the

Copenhagen cryolite processing plant. Cryolite ore contains about 50% fluoride.

Methods: Cancer mortality was determined for the period 1941-1989, and incidence for 1943-1987. For comparison, we used national mortality rates and cancer incidence rates for the Copenhagen area.

Results: Among the men, 300 deaths occurred; 223 were expected. Respiratory (lung and laryngeal) cancers and violent death were responsible for most of this excess; rates for mortality from cardiovascular disease were close to the rates expected. Of the 423 male workers, 119 developed cancers; 103.6 were expected. There was excess incidence of cancers of the lungs (35 men; standard incidence ratio [SIR] = 1.35), larynx (5 men; SIR = 2.29), and urinary bladder (17 men; SIR = 1.84). Maximum incidence occurred after 10-19 years of employment, but otherwise, no stable relationship between cancer incidence and duration of employment was observed. The incidence of respiratory and urinary cancers was particularly high in men less than 35 years old at first employment. Cancers in female workers were too few to allow detailed evaluation.

Conclusions: The increased incidence of respiratory cancers suggests that cigarette smoking was frequent in this cohort, despite the unremarkable cardiovascular mortality, but the disproportionate increase in the incidence of bladder cancer is difficult to explain by smoking habits alone. Because this industrial cohort was exposed to high concentrations of fluoride dust, heavy respiratory exposure to fluoride may have contributed to the increased cancer risk. If these workers inhaled a carcinogenic substance partly excreted in the urine, an increased incidence of respiratory and bladder cancers would not be inconceivable. Implication: The potential role of fluoride as a cause of bladder cancer needs to be explored.

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CLASTOGENIC ACTIVITY OF SODIUM FLUORIDE IN GREAT APE CELLS

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Conflicting evidence has been reported concerning the mutagenicity of sodium fluoride (NaF), especially clastogenicity at concentrations of more than 1 mM. NaF is known to induce chromosome aberrations at these concentrations in human cells, but not in most rodent cells. We considered that such species-specific difference in chromosomal sensitivity would be derived from the phylogenetic distance between rodents and man. To clarify the role of interspecies differences, we investigated the chromosomal sensitivity to NaF in cell lines from various primates, which diverged into many species, including rodent-like prosimians and human-like great apes. The results showed that the clastogenicity of NaF was limited to human and great ape cells.

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SERUM FLUORIDE AS AN INDICATOR OF OCCUPATIONAL HYDROFLUORIC ACID EXPOSURE

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To define the relationship between ionic fluoride concentration in the serum of workers and the amount of hydrofluoric acid (HF) in the work environment, pre- and postshift serum and urine samples of 142 HF workers and 270 unexposed workers were examined. The maximum and minimum concentrations of HF in the air in each workshop varied from the mean by less than 30%. The preexposure levels of serum and urinary fluoride in HF workers were higher ($P < 0.001$) than the control values. This suggests that fluoride excretion from the body continues for at least 12 h. The postshift serum and urinary fluoride concentrations of these workers were significantly higher ($P < 0.001$) than the preshift concentrations. A good correlation ($r = 0.64$) was obtained between postshift serum fluoride and postshift urine fluoride. There was a linear relationship between mean serum fluoride concentration and HF concentration in the workshop. A mean fluoride concentration of 82.3 µg/l with a lower fiducial limit (95 %, $P = 0.05$) of 57.9 mug/l was estimated to correspond to an atmospheric HF concentration of 3 ppm. This is the maximum allowable environmental concentration recommended by the Japanese Association of Industrial Health, and it is also the threshold limit value suggested by the American Conference of Governmental Industrial Hygienists. The results demonstrate that exposure to HF can be monitored by determining the serum fluoride concentration.

COMPARISON OF THE EFFECT OF SODIUM FLUORIDE AND CALCIDIOL ON THE RIB CORTICAL-ENDOSTEAL SURFACE REMODELING IN DOGS RECEIVING PREDNISONE

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The effects of sodium fluoride and calcidiol on the remodeling of the rib cortical-endosteal surface were compared in dogs treated with prednisone over long-term periods. In the study histomorphometric and tetracycline-labeling methods were used. It was found that administration of sodium fluoride in combination with calcidiol and calcium carbonate limited the development of prednisone-induced osteoporosis to a higher degree than treatment with calcidiol and calcium. This included less enhancement of the bone resorption surface, an increase in both the bone formation surface and osteoid seam thickness in conjunction with a lower reduction in the mineralization rate. The changes induced by sodium fluoride had a favorable effect on the ratio of the resorption to the formation processes at the basal multicellular units of bone turnover.

THE MECHANISM OF ALUMINUM-INDEPENDENT G-PROTEIN ACTIVATION BY FLUORIDE AND MAGNESIUM - P-31 NMR SPECTROSCOPY AND FLUORESCENCE KINETIC STUDIES

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With magnesium present, fluoride and aluminum ions activate heterotrimeric G-proteins by forming AlF(x) complexes that mimic the gamma phosphate of a GTP. We report compelling evidence for a newly proposed process of G-protein activation by fluoride and magnesium, without Al^{3+}. With millimolar $Mg_{2}+$ and F^-, G(s) and G(t) activate adenylylcyclase and cGMP-phosphodiesterase, respectively. In P-31 NMR, addition of magnesium to G(i1)alphaGDP or G(t)alphaGDP solutions containing fluoride, but no Al^{3+}, modifies the chemical shift of the GDP beta phosphorus, suggesting that magnesium interacts with the beta phosphate. Titration of this effect indicates that two Mg^{2+} are bound per Galpha. Biphasic activation kinetics, monitored by Galpha tryptophan fluorescence, suggests the rapid binding of one Mg^{2+} to GalphaGDP and the slow association of another Mg^{2+}, in correlation with fluoride binding and Galpha activation. The deactivation rate upon fluoride dilution shows a second order dependence with respect to the residual F^- concentration, suggesting the sequential release of at least three F^-/Galpha. Thus, in millimolar Mg^{2+} and F^-, and without Al^{3+} two Mg^{2+} and three F^- bind sequentially to GalphaGDP and induce the switch to an active $Galpha(GDP-MgF_3)Mg$ state, which is structurally analogous to $Ga(GDP-AlF(x))Mg$ and to $Galpha(GTP)Mg$.

ALUMINUM FLUORIDE INDUCES A REVERSIBLE Ca^{2+} SENSITIZATION IN α-TOXIN-PERMEABILIZED VASCULAR SMOOTH MUSCLE

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The mechanism of aluminum-fluoride (AlF)-induced Ca^{2+} sensitization was explored in α-toxin-permeabilized rabbit mesenteric artery. In the presence of 0.18 μM Ca^{2+} and deferoxamine, a strong chelator of aluminum (Al^{3+}), fluoride (F^-, applied in the form of NaF) induced very slow tension development, while in the presence of tracer levels of Al^{3+}, tension developed rapidly possibly due to formation of Al-F complexes (especially AlF_4^-). As a result, AlF significantly shifted the relationship between tension development and free Ca^{+2} concentration in the Ca^{2+}-EGTA buffer (pCa-tension curve) to the left. The rate of the tension development also depended on the EGTA concentration. The findings suggest that AlF acts on G-protein to enhance Ca^{2+} sensitivity of contractile elements through an H-7-sensitive pathway.

EFFECT OF DELAYED GASTRIC EMPTYING
ON FLUORIDE ABSORPTION IN THE RAT

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The rate and site of fluoride (F) absorption were compared in fasted 350 g male rats given 50 µg F (as NaF) in either water or a 7.5% pectin solution. Absorption was measured at intervals up to 2   h following gastric intubation. Gastric emptying was measured by inclusion of ^{14}C-PEG in the F solution. The extent of gastric F absorption was derived from rates of gastric emptying (^{14}C-PEG loss) and F loss. Pectin markedly slowed gastric emptying, but by 2 h, more than 90% of the solution had passed into the small intestine in both groups, and F absorption exceeded 90% in both groups. The rate of F absorption was initially much slower in the pectin group than in the group given F in water, and plasma F concentration increased more slowly and reached a lower maximum value. Absorption from the stomach was greater in the pectin group, but still accounted for only approx 25% of total gastrointestinal absorption. The reduced rate of F absorption and slower rise in plasma F concentration accompanying delayed gastric emptying indicate that passage of F into the small intestine is the major factor in rapid F absorption.

A STUDY OF THE EFFECT OF HIGH CONCENTRATIONS OF
FLUORIDE ON THE REPRODUCTIVE ORGANS OF MALE RABBITS,
USING LIGHT AND SCANNING ELECTRON MICROSCOPY

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Fluoride was orally administered to rabbits at 10 mg NaF/kg body weight for 18 or 29 months. The animals were then killed and and the structure of the testis, epididymis and vas deferens studied under light and scanning electron microscopes. In animals treated for 29 months, the spermatogenic cells in the seminiferous tubules were disrupted, degenerated and devoid of spermatozoa. In animals treated for 18 or 29 months, loss of cilia on the epithelial cells lining the lumen of the ductus efferentes of the caput epididymidis and of stereocilia on the epithelial cells lining the lumen of the vas deferens was observed. In some regions of the epithelial lining of the lumen of the ductuli efferentes and vas deferens, the boundaries of the cells were not clear and appeared to be peeled off. Mucus droplets were abundant in the vas deferens of control animals, but absent in both the treated groups. Spermatogenesis ceased only in the animals treated for 29 months. The difference in the structural changes observed in the testes of the two treated groups may have been due to the blood-testis barrier. It is concluded that ingestion of high concentrations of fluoride has harmful effects on the male reproductive system.

A MATHEMATICAL MODEL FOR FLUORIDE UPTAKE BY THE SKELETON

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A mathematical model was developed that predicts fluoride accumulation and clearance from the skeleton based upon fluoride bioavailability, bone remodeling rate, and the fluoride binding characteristics of bone. It was assumed that fluoride binds to bone in a nonlinear fashion such that a smaller percentage of fluoride is bound to bone if fluoride intake is increased to high levels. Bone resorption rate was assumed to be proportional to the solubility of hydroxyfluorapatite which is inversely related to bone fluoride content. The predictions made by the model compared favorably with experimental results from fluoride uptake and clearance studies. Parametric studies done using the model showed the following: (1) fluoride can be cleared from the skeleton by bone remodeling, but fluoride clearance takes over four times longer than does fluoride uptake; and (2) fluoride uptake by the skeleton was positively associated with bone remodeling rate. formed bone does not decrease with reduced remodeling rates and surpasses 10,000 ppm for intakes of fluoride greater than 9 mg/day. For osteoporosis, daily dose and duration of fluoride treatment should be selected to avoid reaching a toxic cumulative bone fluoride content.

BONE HYPERTROPHY AND TRABECULAR GENERATION IN PAGET'S DISEASE AND IN FLUORIDE-TREATED OSTEOPOROSIS

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The replacement of lost trabeculae characteristic of postmenopausal osteoporosis is problematic, since a biological pathway has not been established for trabcular regeneration *de novo* in the healthy, intact, mature skeleton. Possible pathways for trabecular replacement may occur under pathological conditions, in particular those associated with bone hypertropy. The topography of trabecular hypertrophy was compared in two groups of subjects with disease- or treatment-induced osteosclerosis following a period of atrophy. In Paget's disease and fluoride-treated osteoporosis a thickening of rarefied trabeculae in both was associated in Paget's disease only with an increase in the trabecular number and the transformation of a discontinuous arrangement into a more continuous network. The sequence seems to be a progression intratrabecular resorption normally attendant upon a period of trabecular thickening. The failure of fluoride-treated bone in this respect, due to the unusual stability of the fluorotic skeleton, may provide insight to more effective anabolic regimens.

INVITRO EXPOSURE TO SODIUM FLUORIDE DOES NOT MODIFY ACTIVITY OR PROLIFERATION OF HUMAN OSTEOBLASTIC CELLS IN PRIMARY CULTURES

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The anabolic effects of sodium fluoride (NaF) on trabecular bone mass in osteo-porosis is now well established. In vivo histologic studies performed in humans and other animals have shown that fluoride induces an increase in osteoblast number at the tissue level. To determine the mechanisms of action of fluoride on osteoblasts, we studied the effects of NaF on short- and long-term cultures of human osteoblastic cells derived from bone explants obtained from 21 donors. In short-term experiments, bone-derived cells were exposed to NaF for 4 days. At doses ranging from $10(-11)$ to $10(-5)$ M, NaF did not modify the alkaline phosphatase (AP) activity or osteocalcin secretion. In long-term experiments, half the bone samples from 15 donors were cultured for 4 months in the presence of $10(-5)$ M NaF and the other half were maintained in NaF-free medium. Observations by light and electron microscopy disclosed no morphologic modification in bone explants after 4 months of exposure to NaF, despite an increase in the bone fluoride content. After the first month of culture, slight but not significant increases were noted in 6 of 10 cases for AP activity, 4 of 10 for osteocalcin secretion, and 5 of 7 for [H-3]thymidine incorporation. After 4 months of culture in the presence of NaF, no change in AP activity or cell proliferation was noted. In contrast, the osteocalcin secretion significantly decreased ($p < 0.05$). These data suggest that, *in vitro*, under the conditions of this study, there is no direct effect of fluoride on the proliferation or activity (AP activity and osteocalcin secretion) of human osteoblastic cells and that this effect is very likely mediated by a cofactor.

X-RAY MICROANALYSIS OF FLUORIDE DISTRIBUTION IN MICROFRACTURE CALLUSES IN CANCELLOUS ILIAC BONE FROM OSTEOPOROTIC PATIENTS TREATED WITH FLUORIDE AND UNTREATED

Georges Boivin, Brigitte Grousson and Pierre J Meunier
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Fluoride is able to augment cancellous bone mass in vertebral osteoporosis but is responsible for osteoarticular side effects in which microfractures are thought to be involved. During healing of these microfractures, a callus is formied all around the cancellous fracture line. Our hypothesis is that in fluoride-treated osteoporotic patients, calluses are bone sites where fluoride is focally deposited at a high concentra-tion, and this could induce a local defect of calcification with a poor healing of microfractures. Our aim was to validate this hypothesis on several calluses following

microfractures in undecalcified iliac cancellous bone from six women with osteo-porosis (four fluoride treated and two untreated). Histologically normal iliac cancellous bone tissue, taken from a subject having neither fluoride treatment nor microfracture, was also examined. Selected areas, including new woven bone (calluses) and old lamellar bone, were carbon-coated and analyzed using an electron microprobe. Fluoride K_α and calcium K_α radiations were detected with wavelength and energy-dispursive spectrometers, respectively. In old lamellar bone at a distance from microfractures, the fluoride level was similar in normal and untreated osteo-porotic patients but was slightly increased in treated osteoporotic patients. In un-treated osteoporotic patients, the fluoride level was slightly higher (about 1.2 times) at the site of microfractures (lamellar and woven bone) than in lamellar bone far from such fractures, but fluoride was homogeneously distributed in lamellar and woven bone. In contrast, in treated osteoporotic patients, fluoride content was much higher (about 1.7 times) at the site of microfractures (lamellar and woven bone) than in lamellar bone far from fractures, but fluoride was heterogeneously distributed within the calluses, with the highest level in woven bone and the smallest in adjacent lamellar bone. The present data demonstrate that fluoride is preferentially concentrated in calluses of cancellous microfractures in fluoride-treated osteoporotic patients. It is likely but remains to be proven that this focal increase in fluoride uptake compromises the healing of microfractures.

Key words: Cancellous Iliac bone; Fluoride; Osteoporosis; X-ray microanalysis.

Reprints: Dr Georges Boivin, INSERM Unité 234, Faculté A Carrel, Lyon, France.

THE EFFECTS OF PROTEIN DEFICIENCY AND FLUORIDE ON BONE MINERAL CONTENT OF RAT TIBIA

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This study examined the effects of chronic protein deficiency and fluoride administration (10 mg/kg/day), separately or in combination, on rat tibia properties. Protein deficiency increased the bone fluoride concentration and reduced the bone mineral content (BMC) especially at the proximal or growing end which which contains mainly cancellous bone. Fluoride administration also reduced BMC, but to a lesser extent, and it resulted in proximal tibia fluoride concentrations that were nearly twice those of the distal tibia. The interaction between fluoride administration and the protein content of the diet on BMC was nonsignificant, suggesting that the effects were additive, not multiplicative or synergistic. Fluoride administration, but not protein deficiency, increased bone magnesium levels. It is hypothesized that the reduction in BMC in the areas where the fluoride concentrations were the highest was due to a localized toxic effect of fluoride.

Key words: Acid-base status; Fluoride; Magnesium; Metabolism; Photon absorptiometry; Toxicity.

Reprints: Dr G M Whitford, Department of Oral Biology, School of Dentistry, Medical College of Georgia, Augusta, Georgia 30912-1129, USA.

STIMULATION OF BONE FORMATION IN OSTEOPOROTIC PATIENTS TREATED WITH FLUORIDE ASSOCIATED WITH INCREASED DNA SYNTHESIS BY OSTEOBLASTIC CELLS *IN VITRO*

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In this study we evaluated whether the fluoride-induced increased bone formation in osteoporosis is mediated by stimulation of bone cell proliferation and/or differentiation. We analyzed the kinetics of DNA synthesis and the phenotypic features of osteoblastic cells isolated from the trabecular bone surface in relationship to histomorphometric indices of bone formation evaluated on the same bone biopsy in 12 osteoporotic patients treated with fluoride. Osteoblastic cells isolated from patients with a higher than normal bone formation rate, increased mean wall thickness of trabecular bone packets, and high trabecular bone volume after fluoride therapy displayed a higher than normal rate of DNA synthesis *in vitro*. The peak of [^{3}H]thymidine incorporation into DNA, the maximal DNA synthesis, and the area under the growth curve of osteoblastic cells isolated from these patients were higher than the values in normal bone cells obtained from age-matched controls. By contrast, *in vitro* parameters of osteoblastic cell proliferation were not different from normal in fluoride-treated osteoporosis patients in whom bone formation was not increased, although the duration of treatment and bone fluoride content were not different. Parameters of bone cell proliferation *in vitro* were increased in correlation with the mean wall thickness, and the latter correlated with the trabecular bone volume, indicating that the augmentation of bone formation and bone volume induced by fluoride was paralleled by an increased proliferation of osteoblastic cells. Basal osteocalcin production (corrected for cell protein) and alkaline phosphatase activity *in vitro* were comparable, and the response to 1,25-dihydroxyvitamin D_3 (10 nmol/liter, 48 h) was not different in normal osteoblastic cells and in cells from fluoride-treated osteoporosis patients whether they had high or normal bone formation. The results show that the fluoride-induced increased bone formation in osteoporotic patients is associated with an increased *in vitro* proliferative capacity of osteoblastic cells lining the trabecular bone surface, whereas parameters of osteoblast differentiation are not affected. The data also suggest that induction of a higher than normal bone cell proliferation is prerequisite for the stimulation of bone formation by fluoride.

PREVENTION OF OSTEOPOROSIS: CURRENT RECOMMENDATIONS

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Osteoporosis and its treatment have attracted much attention in recent years, especially since the widespread recognition of its association with the menopause.

The resulting fractures are a cause of considerable morbidity and mortality in the elderly, and current costs of treating these patients has been estimated to be in excess of 500 Pounds million per annum in the UK. As the causes of osteoporosis are now

recognised the condition may be largely preventable, especially in women, and significant saving in health expenditure could be made if preventive methods are applied to those most at risk. The most well researched preventive treatment for osteoporosis is hormone replacement therapy (HRT) which offers additional benefits to those who choose it. Alternative methods currently under investigation for those who cannot or will not use HRT include those agents which inhibit the resorption of bone and those that stimulate the production of new bone.

Treatment of established disease, *i.e.* attempts at increasing bone density in those with significant loss, is more difficult and methods so far investigated are not without risks and adverse effects. Furthermore, whether an increase in bone mineral density results in a reduced rate of fracture incidence has yet to be confirmed.

Key words: Fluoride treatment; Fracture rate; Estrogen replacement therapy; Osteoporosis; Postmenopausal bone loss; Postmenopausal women.

ALUMINOFLUORIDE ACTIVATES HYPERPOLARIZATION-ACTIVATED AND STRETCH-ACTIVATED CATIONIC CHANNELS IN SINGLE SMOOTH MUSCLE CELLS

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Aluminofluoride (AF) has a variety of biological actions such as activation of GTP binding proteins and inhibition of phosphatases. In the present study, the effects of AF on hyper-polarization- and stretch-activated cationic channels (HA-SACs) were investigated in isolated gastric smooth muscle cells from the toad, *Bufo marinus*, using the patch-clamp technique. In cell-attached patches extracellular application of AF (20 mM KF plus 20 μM $AlCl_3$) reversibly increased HA-SAC activity without changing its voltage sensitivity. The single channel current amplitude of HA-SACs was not affected during this procedure. The mechanism of AF-induced activation of HA-SACs remains unclear. However, this activation may play a role in contraction of smooth muscle induced by AF.

Key words: Patch-Clamp technique; Smooth muscle cells; Aluminum; Fluoride; Ion channels.

EFFECT OF FLUORIDE DOSAGE ON BONE DENSITY, SONIC VELOCITY, AND LONGITUDINAL MODULUS OF RABBIT FEMURS

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Relationships between the fluoride dosage administered to weanling New Zealand white male rabbits and some mechanical properties of the compact bone were investigated for a wide range of dosages. The measured quantities were density, longitudinal sonic velocity in the radial direction, and fluoride ion concentration in compact bone. The longitudinal elastic modulus was estimated from the product of the density and the square of the sonic velocity. The relative static load stress was estimated from the ratio of the final body weight to the cross-sectional area of the femur. These measurements and derived quantities provide quantitative measures of bone quality. A slight peak (2% greater than reference) was determined for the density and a slightly larger peak (5% above reference) for the longitudinal sonic velocity at a dosage of approximately 20 mg/kg/day. The longitudinal elastic modulus exibited a substantial peak, 14% greater than reference. The relative static load stress showed a very slight peak as a function of dosage and also as a function of fluoride concentration in the bone. When plotted against the elastic modulus, a nonlinear monotonic increase was observed with modulus, showing that the cross-sectional area of the bone is responsive to the stiffness of the tissue. Stiffer tissue produces a smaller cross section, whereas a more compliant tissue requires a marked increase in the area. There appears to be an improvement of bone quality for low fluoride dosage which tends to be masked by biological variability. The derived quantities, longitudinal elastic modulus, and relative static load stress provide the clearest demonstration of the improvement. There is marked deterioration for higher dosage. The conclusions are limited by a need to relate the properties of rabbit to human bone, and young growing bone to older osteoporotic bone.

TOPICAL APPLICATION OF FLUORIDES ON TEETH:
NEW CONCEPTS OF MECHANISMS OF INTERACTION

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Prevention of caries in exposed root surfaces constitutes an important clinical problem. It is thus important that clinicians involved with periodontology have an insight into fluoride prophylaxis. The understanding of the cariostatic mechanism of fluoride has improved during recent years. The aim of the present review is to give a short account of the present concept. Calcium fluoride appears to be the only product which is formed on enamel, dentin or cementum during brief topical treatments with fluoride or use of toothpaste containing fluoride. This calcium fluoride is stable in the oral environment; this is contrary to what was believed until recently. The calcium fluoride constitutes a pH-dependant reservoir of fluoride which releases fluoride when pH drops. The practical consequences of this concept are discussed.

DRINKING WATER FLUORIDATION AND CARIES PROPHYLAXIS:
WITH SPECIAL CONSIDERATION OF THE EXPERIENCE
IN THE FORMER EAST GERMANY

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Drinking water fluoridation for caries prophylaxis is not a means of primary prevention: *i.e.*, avoidance of sugar and microorganisms in the oral cavity; but rather a means of secondary prevention: *e.g.*, prevention of bacterial production of carboxylic acid from sugar, and therapy: *e.g.*, enhancement of enamel resistance to demineralization by incorporation of fluoride in remineralization of the enamel surface.

Currently available epidemiologic studies on the effects of drinking water fluoridation reveal: reduction of the incidence of caries, particularly in children no detrimental health effects; cosmetically undesirable dental fluorosis may occur, however.

Nevertheless, introduction of drinking water fluoridation in Germany is not recommendable because of: the greater effectiveness of primary caries prevention, the acceptance of which is reduced, however, by drinking water fluoridation the at least equal prophylactic effect of fluoride via other routes, *e.g.* via toothpaste the narrow range between beneficial and detrimental dosage the avoidance of fluoride-enriched waste water the prerogative of minimal manipulation of drinking water content.

FLUORIDE SUPPLEMENTATION - A SURVEY OF PEDIATRICIANS AND PEDIATRIC DENTISTS

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Objective. To determine the protocol and use of prescriptions of fluoride supplementation by primary care pediatricians and pediatric dentists in the Houston (Tex) area.

Design. Survey mailed to all primary care pediatricians and pediatric dentists listed in the Yellow Pages of the Greater Houston telephone directory.

Participants. 153 pediatricians and 47 pediatric dentists.

Main Results. Ninety-six percent of the participants prescribed fluoride supplements. Fifty-one percent of the pediatricians and 61% of the dentists considered that the fluoride content of the water was important. Seventy percent of the pediatricians and 30% of the dentists discontinued the use of supplements by age 7 to 10 years.

Conclusions. Pediatricians and pediatric dentists should consider the need for water analysis prior to supplementation and should continue the use of fluoride supplements until 16 years of age.

KeyWords: Fluoride supplements; Pediatricians; Pediatric dentists.

FLUORIDE ACQUISITION ON AND IN FLUOROTIC HUMAN ENAMEL AFTER TOPICAL APPLICATION *IN VITRO*

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The uptake of alkali soluble and alkali insoluble fluoride on and in fluorotic April enamel was investigated in vitro. Teeth from Kenya, assigned score 3 in accordance with Thylstrup-Fejerskov's fluorosis index, were used. The enamel was treated with either a neutral 2% NaF solution, a 0.2% NaF solution (pH 5.5), or the supernatant from a 0.1 % NaF-containing toothpaste (pH 7). The treatment time was 1 h. The reaction product formed on the enamel was analyzed by KOH extraction and acid etching. Significantly higher amounts of alkali soluble fluoride were formed on the enamel from the 2% and 0.2% NaF solutions, as compared with the control. There was also a significant increase in the firmly bound fluoride after treatment with the neutral 2% NaF solution.

Key words: Calcium fluoride; Dental fluorosis; Fluorapatite; Preventive dentistry; Sodium fluoride.

FLUORIDE CONCENTRATIONS IN UNERUPTED FLUOROTIC HUMAN ENAMEL

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Unerupted fluorotic human enamel was obtained from teeth surgically removed from patients with dental fluorosis. Fluoride was measured in samples produced by serial acid etching from the surface to the interior of blocks of buccal and lingual enamel. The severity of fluorosis, according to the TF index, was determined from the macroscopic and microradiographic appearance of the specimens. The shape of the fluoride profiles was not affected by the degree of severity of fluorosis, but the fluoride concentrations increased with increasing severity of lesions. Fluoride concentrations were similar to those previously recorded in erupted fluorotic enamel and were not related to the length of time the teeth had been present in the jaws. It was concluded that the fluoride content of erupted fluorotic enamel represents fluoride acquired during tooth formation and that further uptake prior to eruption may be negligible.

EFFECT OF FLUORIDE ON CARIES PROGRESSION AND DENTIN APPOSITION IN RATS FED ON A CARIOGENIC OR NON-CARIOGENIC DIET

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The effect of fluoride in drinking water on the progression of dentinal caries and dentin apposition was studied in Wistar rats. The initiation of enamel caries lesions was first induced for 2 wk with S. sobrinus and a 43% sucrose diet after weaning. Thereafter the animals were fed on either a cariogenic or a non-cariogenic diet and distilled water supplemented with 0, 1, 7 or 19 ppm fluoride. The areas of dentinal caries and dentin apposition were quantified after tetracycline staining. Fluoride reduced dentinal caries progression after the initiation of lesions in the presence of a cariogenic diet at a concentration of 19 ppm F, and without sucrose at 1 ppm F. The effect of fluoride in reducing dentin apposition with a cariogenic diet was dose-dependent, whereas fluoride in non-cariogenic groups had practically no effect on dentin formation. These results suggest that fluoride together with a high concentration of sucrose in the diet might have an odontoblast-mediated effect on the regulation of the progression of dentinal caries.

PREDICTION OF ROOT CARIES IN PERIODONTALLY TREATED PATIENTS MAINTAINED WITH DIFFERENT FLUORIDE PROGRAMMES

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The aims of the investigation were to evaluate the effect of different fluoride programmes, as adjuncts to professional plaque control every 3-4 months, on root caries incidence in periodontally treated patients and to identify risk factors for root caries development. Ninety-nine individuals, 33-76 years old, who had been treated for periodontal disease were subjected to one of three fluoride programmes during a 2-year period: (1) professional application, 3-4 times/year, of Duraphat(R) (n = 34) or (2) of a 0.4% stannous fluoride gel (n = 33), or (3) daily mouthrinsing with a 0.05% sodium fluoride solution (n = 32). A number of clinical recordings and laboratory tests, used as presumptive risk indicators for root caries,were carried out before and on three different occasions after the periodontal treatment. No statistically significant differences were found between the various fluoride programmes. During the 2-year period, a total of 246 new decayed or filled surfaces (DFS) were recorded, 72 (29.3%) of which were diagnosed as active and 124 (50.4%) as inactive root caries lesions; 50 (20.3%) of the surfaces had been restored. Individuals with greater-than-or-equal-to 1 new root DFS during the 2 years (n = 50) differed significantly from those with 0 new root DFS (n = 49) as concerns salivary counts of mutans streptococci and lactobacilli, root plaque scores and percentage of exposed root surfaces. Baseline root caries prevalence (r = 0.43) and root plaque scores (r = 0.36) showed the highest correlations with new root DFS. By stepwise multiple regression analysis, it was shown that these two variables contributed significantly to the variance of root caries incidence (new DFS) during the 2-year period. Smokers had a significantly higher root caries prevalence at baseline and higher root caries incidence during the study than non-smokers.

DENTINOGENESIS AND THE CALCIOTRAUMATIC RESPONSE TO THE INJECTION OF LEAD OR FLUORIDE IONS

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A number of ions can disturb the formation of dentine resulting in a calcio-traumatic response. The calciotraumatic response following the injection of sodium fluoride was investigated using backscattered electron imaging in the scanning electron microscope and compared with the response to lead acetate. With fluoride, there was formation of a hypermineralized band succeeded by a relatively hypomineralized band, but with lead acetate, only a hypomineralized band was produced. However, there were some differences in the response between the labial and lingual dentine with both

ions. In the labial dentine following injection of sodium fluoride, the onset of hypermineralization was less abrupt than in the lingual dentine. Furthermore, the transition from hypermineralization to relative hypomineralization was more abrupt in the labial dentine. Sometimes there was an increased thickness of labial dentine between the hypermineralized layers towards the apex of the tooth and this dentine was less homogeneously mineralized. Normal incremental lines were occasionally seen both labially and lingually. Lead acetate produced a more severe disruption of dentine formation labially than lingually. These differences in response may be related to the pattern of mineralization labially and lingually and to the systemic effects following the injection of sodium fluoride.

URINARY FLUORIDE EXCRETION IN CHILDREN USING POTASSIUM FLUORIDE CONTAINING SALT OR SODIUM FLUORIDE SUPPLEMENTS

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With the introduction of fluoridated domestic salt in France in 1986, questions have arisen with respect to its efficacy in caries prevention. It has been of interest to compare the urinary excretion of fluoride in children who consume fluoridated salt to that in children who take fluoride tablets. Ninety-three schoolchildren, 10-14 years of age, participated in the study and were divided into four groups: group I consumed fluoridated salt with every meal; group II ate at a school restaurant once a day and consequently consumed fluoridated salt at only their evening meal, as fluoridated salt is not authorized for use in collective restaurants; group III consisted of children taking fluoride tablets (1.0 mg F/day) exclusively, and group IV did not receive any systemic administration of fluoride for prevention and constituted a low-fluoride control group. Total 24-hour urine samples were collected from all subjects. The average daily urinary flow rates varied from 0.51 to 0.68 ml/min, but showed no statistically significant differences among the groups. The average urinary fluoride concentrations were 0.60, 0.30, 0.99, and 0.28 mg/l, respectively, for groups I-IV. The mean 24-hour urinary fluoride concentrations and excretion rates for children who consumed fluoridated salt at all meals (group I) were not statistically different from those using tablets (group III). There were also no statistically significant differences between groups II and IV. The differences between urinary fluoride concentrations and excretion rates of groups I and III, as compared with group IV, were statistically significant.

INFLUENCE OF OCCLUSION ON THE FLUORIDE DISTRIBUTION IN RAT MOLAR CEMENTUM

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This study was undertaken to examine the influence of occlusion on the fluoride distribution in cementum following an experiment in which the occlusion in rats was locally altered by extracting the upper left molar. These and control rats with normal occlusion were given water containing 0 or 100 ppm fluoride for 12 weeks. The fluoride distributions in cementum from both first lower molars of the same animal were compared. The fluoride concentrations had increased throughout the tissue as a result of increased fluoride administration, irrespective of any changes in occlusion. They were, as usual, generally highest at or near the cementum surface and decrease towards the interior of the tissue. Where there had been a change in occlusion, the thickness of cementum was less than that of the contralateral tooth, but, despite this, the fluoride profiles in contralateral teeth were similar in both experimental and control rats. In the experimental rats, on the other hand, the total fluoride tended to be lower, and the mean fluoride tended to be higher in left molars without antagonists. These findings were never seen in the control rats. It was concluded that the alteration in occlusion influenced the fluoride distribution in the cementum through its effect on the rate of cementum formation.

ENAMEL AND PLAQUE FLUORIDE FOLLOWING GLASS IONOMER APPLICATION *INVIVO*

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Glass ionomer fillings have been suggested to act as a fluoride-releasing system in the mouth. The aim of the present study was to evaluate whether a glass ionomer slab applied on the enamel can increase the fluoride content of the enamel and plaque of adjacent teeth in real-life conditions with frequent exposure to fluoride from other sources. Twenty-five adults living in a town with fluoridated drinking water participated in the study. The initial enamel fluoride content on the buccal surface of the contralateral premolars was determined using the acid etch biopsy technique. A round glass ionomer slab was placed buccally on the first molar on a randomly chosen side of the mouth (test side). After 2 weeks, the enamel fluoride content of premolars on the test and control sides was again determined whilst avoiding the site of the first biopsy. In addition, one biopsy was made on a previously etched area. After 2 and 4 weeks, plaque was collected from three approximal surfaces both on the test and control side, and the total fluoride content of the plaque, was analysed. There were no

significant differences in the fluoride content of sound or etched enamel before and after placement of glass ionomer. The fluoride content of approximal plaque of teeth close to glass ionomer was not higher than that of the control teeth, after either 2 or 4 weeks. Using the present method, no increase in the fluoride level of teeth adjacent to glass ionomer could be demonstrated. This may be due to the masking effect of fluoride from other sources.

SECONDARY CARIES *INSITU* AROUND FLUORIDE-RELEASING LIGHT-CURING COMPOSITES - A QUANTITATIVE MODEL INVESTIGATION ON 4 MATERIALS WITH A FLUORIDE CONTENT BETWEEN 0 AND 26 VOL-PERCENT

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In the literature, secondary caries around composite restorations is reported often. Fluoridated composites are therefore interesting materials because they might reduce or inhibit secondary caries. In this article an in situ model investigation is presented in which the effect of F-releasing composites on enamel demineralisation around an artificial gap of 200 μm width was quantified after 1 month. The fluoride content of the composites varied between 0 and 26 vol%. The beneficial effect of the fluoride released was larger in the gap than at the outer enamel surface. In the gap, all fluoridated composites reduced the enamel demineralisation statistically significantly with respect to the non-fluoridated control. Microradiography showed a reduction of lesion depth values of 27-45%, and a reduction of mineral loss values of 25-56%. At the outer enamel surface next to the artificial gap, a beneficial fluoridation effect was measurable only near the most fluoridated composite. The results indicate that fluoridated composites may play a role in the future prevention of secondary caries.

EXPOSURE TO LOW LEVELS OF FLUORIDE AND DENTAL CARIES IN DECIDUOUS MOLARS OF TANZANIAN CHILDREN

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In general, the prevalence of caries in African children may be classified as low to very low. In order to reduce this level even further, methods including the practice of good oral hygiene and administration of fluoride, *e.g.* water fluoridation, have been suggested. In 1984, 1986 and 1988, a mixed-longitudinal study amongst schoolchildren

was carried out in a rural and urban area of Tanzania. In the rural area, shallow wells had been constructed at different periods in time in eight villages since the late 1970s. The drinking water in three of the villages contained fluoride in the range of 0.5-0.8 ppm (fluoridated) and contained less than 0.4 ppm fluoride in the remaining five villages (non-fluoridated). These fluoride levels were disclosed to the authors only during the course of the study. Thus the data were reanalysed to investigate the effects of fluoride and length of fluoride exposure on caries experience in the deciduous dentition. The study was carried out amongst 522 7- and 8-year-olds. Fluoride tablets were not used and toothpaste was virtually unavailable. Three periods of fluoride exposure were identified, *i.e.* 3, 5 and 7 years. The outcome variable was the mean dmft score in deciduous molars whereas the explanatory variables were age, length of fluoride exposure and year of investigation. Nutrition was considered a co-variate. Analysis of co-variance revealed a fluoride effect ($p = 0.0004$). Regression analysis did not show significant relationships between the mean dmft score and the three periods of fluoride exposure. The findings indicated that 3 years' exposure to low fluoride levels in drinking water can reduce further low caries severity levels in deciduous molars.

CARIES INCIDENCE, MUTANS STREPTOCOCCI AND LACTOBACILLI IN IRRADIATED PATIENTS DURING A 12-MONTH PREVENTIVE PROGRAMME USING CHLORHEXIDINE AND FLUORIDE

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London, England

Radiotherapy (RT) near salivary glands results in changes in the oral flora in favour of cariogenic organisms and an increased susceptibility to caries. The aim of this study was to assess the effect of a 12-month preventive programme on caries incidence and on the levels of mutans streptococci (ms) and lactobacilli in tongue loop samples taken from patients before, during and after RT. The regime consisted of 2 x daily rinsing with 10 ml 0.2% chlorhexidine, diluted 1 : 1 with water, for 1 week before RT, during RT and for 4 weeks after RT. This was then substituted with a 0.05% NaF rinse daily. A saliva substitute containing 2 ppm F was used as required. Scaling was carried out before RT and dietary advice and oral hygiene instruction given. Appropriate radiographs were taken at baseline and after 6 and 12 months. Tongue loop samples for microbiology were taken in the middle and end of RT and subsequently at 6,8,12,24, 40 and 52 weeks. Whenever levels of ms exceeded $2 \times 10(5)$ cfu/Ml sample, 1% chlorhexidine gel in custom-made applicator trays was applied by the subject for 5 min daily for 14 days. In 25 subjects completing the

programme, there was a total of 3 new caries lesions after 12 months. Thirteen pre-existing enamel lesions were arrested. There were significant reductions ($p < 0.005$) in ms levels from baseline values during RT and 4 weeks after RT. There were no significant increases in ms levels throughout the study. Nineteen of the 25 subjects required at least one course of chlorhexidine gel to maintain this low level of ms. Lactobacilli levels rose steadily after RT and remained high throughout the study. There was a significant improvement in gingival health at 6 months ($p < 0.005$) and at 12 months ($p < 0.05$). Mean stimulated whole salivary flow rate was significantly reduced ($p < 0.05$) after RT; this reduction persisted for 12 weeks and did not return to baseline values at the end of 12 months. It is concluded that the chlorhexidine/fluoride regime used in this study can be recommended for the control of caries in this group of highly susceptible individuals.

POTENTIOMETRIC TITRATION OF FLUORIDE USING AN ALUMINIUM WIRE INDICATOR ELECTRODE

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Despite the great possibilities aluminium wire electrodes are seldom used in electroanalytical techniques. Fabrication of an aluminium wire electrode is difficult and is described in detail. The proper pre-treatment for the aluminium wire electrode was found to be cathodization in sulfuric acid $(1 + 3)$. In the plot of potential versus pF^-, linearity was obtained down to $10(-6)$ mol l-1 with a slope of 62 mV. Equimolar titrations of F^- versus La^{3+} were carried out in aqueous solutions down to a level of $10(-6)$ mol l-1, at which the curve height obtained was only 6 mV at pH 2.0. All height obtained was only 6 mV at pH 2.0. All titrations were carried out in the presence of $10(-4)$ mol l-1 $NaClO_4$. None of the other halides interfered. In 50% methanol and ethanol the titration could be carried out at $10(-9)$ mol l-1 F^-, pH 2.0, the curve heights obtained being 17 and 10 mV, respectively. The performance of the aluminium wire electrode was found to be far superior when compared with the performance of a fluoride ion-selective crystal membrane electrode, especially for titration. Water samples were analysed at the sub-ppm level.

Dear Dr Colquhoun

Concerning your Editorial in Vol.25 No.4 1992: We understand the ISFR policy of "No Politics." Yet it is economic-political pressure which gets in the way of honest scientific research. The relationship of accumulating scientific data to the continuing "promotion" of water fluoridation has to be faced somehow, someway.

Congratulations for a fine job of editorship.

Herbert H Robinson DDS
St Petersburg, Florida, USA

Corrected Abstract
The first two lines of page 76 of most printings of our last issue (Vol.26 No.1) were jumbled, making the latter part of the Abstract largely unintelligible. The following is the correct version.

DOES THE NAKED FLUORIDE ION EXIST?

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Of couse the naked fluoride ion does not exist in a chemical environment, just as no free proton is stable in a chemical environment. The potential usefulness of a naked fluoride ion is apparent: whereas H^+ or the closest to it, the magic acids, are extremely acidic, F^- would be extremely basic with immense catalytic properties. Methods of approximating a naked fluoride ion are described and discussed. Recently two fluorides that can easily be prepared in every laboratory became accessible. Even more important, the chemical properties of the cations of these fluorides are complimentary. The field is now wide open - studies on C-C bond formation, formation of carbanions, elimination and condensation reactions, silylation and desilylation, and cyclization, each with stoichiometric or catalytic amounts of F^-, is possible. Finally it is noted that many physicochemical properties of F^- need to be redetermined, since without doubt the almost naked F^- ion differs substantially from the hydrated F^- ion.

Keywords: Cations; Cesium effect; Fluoride ion

INSTRUCTIONS TO AUTHORS

1. **General.** The submitted paper, with a copy, should be written concisely in English. Either American or British spelling is accepted. Double space with generous margins. Measures should be in metric system.

2. **Title.** A concise but informative title should be followed by the name(s) of the author(s). The address where the research was carried out should appear at the bottom of the first page.

3. **Summary.** Begin with a brief factual summary.

4. **Key words.** List the major themes or subjects.

5. **Introduction.** State the reason for the work with a brief review of previous work on the subject.

6. **Materials and Methods.** Condense. However, if the methodology is new or developed by the author(s) it can be more detailed.

7. **Results.** List the direct conclusions of the work.

8. **Discussion.** Deal with general conclusions, referring to other work on the subject. In short papers Results and Discussion may be combined.

9. **Abbreviations or Acronyms.** Define, either in brackets or in footnotes, when they first appear.

10. **Acknowledgements.** Keep brief. They may include funding source, technical assistance, text editing and useful comments.

11. **References.** See current issues of journal for usual style, which identifies references by bracketed numbers in the order in which the references first occur. Other styles may be accepted, provided they are accurate and consistent.