Fluoridated Water, Skeletal Structure, and Chemistry

ERVING F. GEEVER, M.D., HAROLD G. McCANN, M.S., FRANK J. McCLURE, Ph.D., WILLARD A. LEE, B.S., and ELLIOTT SCHIFFMANN, Ph.D.

THE hazard to the skeletal tissue of excess fluoride was clearly described in the classic studies of Roholm (*1*). Concomitant with sclerosis and extensive calcification, the bones accumulate an intolerable quantity of fluoride. Roholm's observations, adequately confirmed by other studies, emphasized the toxic potential of fluoride when the limit of skeletal tolerance is exceeded. Thus, the possibility of bone damage from prolonged use of fluoridated drinking water (1.0 ppm of fluoride) has been extensively studied. This trace quantity of fluoride in water, however, has no adverse affect on skeletal tissues (*2*).

In contrast to the toxic potential of fluoride, a benign effect on skeletal health from drinking a highly fluoridated water has been suggested. Observations on residents of Bartlett, Tex., where there was 8.0 ppm of fluoride in the water (*3*), gave evidence that osteoporotic bone changes in the aged were less frequent than would have been expected.

In the early 1960's, the clinical use of fluoride in relatively large quantities was reported to have some value in the treatment of osteoporosis (*4–8*).

In 1966, a substantial epidemiologic survey also provided evidence that a skeletal benefit had resulted from prolonged ingestion (essentially a lifetime) of drinking waters containing from 4.0 to 5.8 ppm of fluoride (*9*). A control group in this study used drinking waters containing 0.15–0.30 ppm of fluoride. Comparisons between the two groups, based essentially on bone density,

Dr. Geever is professor of pathology in the department of pathology of Albert Einstein College of Medicine, Yeshiva University. Mr. McCann (deceased) was a staff member of the Institute of Research and Advanced Study in Dentistry, Forsyth Dental Center, Boston, Mass. Dr. McClure, who at the time of the study was chief of the Laboratory of Biochemistry, National Institute of Dental Research, Bethesda, Md., is now retired but continues at the institute as a guest worker. Mr. Lee is a chemist and Dr. Schiffmann a biochemist in this laboratory. Tearsheet requests to E. F. Geever, M.D., Department of Pathology, Albert Einstein College of Medicine, Eastchester Road and Morris Park Ave., Bronx, N.Y. 10461.

collapsed vertebrae, osteophytic changes, and bone disease, indicated that 4.0–5.8 ppm of fluoride in the drinking water had decreased the prevalence of osteoporosis. A mild positive calcium balance and a reduced urinary excretion of calcium suggested recalcification of the skeletal tissues.

Korns evaluated the effect of the fluoridated water of Newburgh, N.Y. (1.0–1.2 ppm of fluoride) and of Kingston, N.Y. (0.05 ppm of fluoride) on the incidence of hip fractures in persons over 40 years of age, as listed in hospital records (*10*). In addition, cases of wrist fracture were ascertained from X-ray facilities in the two communities. The data, however, did not reveal significant differences between the two communities. Additional data on the age-specific and sex-specific prevalence of osteoporosis and of collapsed vertebrae in persons over 55 years of age who had lived 22 or more years in one of these cities (210 persons from Kingston and 219 from Newburgh) also did not reveal differences between the two communities. There was no indication that the fluoridated water affected the skeleton. The author concluded that "A more meaningful research design is needed to assess whether a community water level of 1.0 ppm of fluoride has any effect on the prevalence and severity of osteoporosis."

Major interest centers on, and important data pertain to, the quantity of fluoride in drinking water in relation to the fluoride in bones and in relation to bone disease. Extensive previous studies (*11–13*) have given no evidence of adverse quantities of skeletal fluoride nor of pathological changes even when the drinking water contained as much as 8.0 ppm of fluoride, as in Bartlett, Tex. Our study provides data on the quantity of fluoride in the skeletal tissues of residents of Grand Rapids, Mich., and the microscopic structure of these tissues after prolonged consumption of the city's fluoridated water.

Material and Methods

Material. Specimens of vertebrae, ribs, and the abdominal aorta taken at autopsy constituted the material of our study. These specimens were analyzed for ash, calcium, and fluoride; a complete microscopic examination was also performed. Specimens from the bodies of the deceased who had resided in Grand Rapids were compared with control specimens obtained at necropsies performed in New York City and Albany, N.Y., cities where fluoride in the drinking water was of the order of 0.1 ppm or less. The residential histories of the deceased were verified in most instances, as were their ages at death and the cause of death. The Grand Rapids specimens came from the bodies of persons who had used the fluoridated water of that city for a maximum of 20 years.

Data on the fluoride present in human bones may contribute indirectly to resolving the question of whether fluoridated water might help control osteoporosis. Obviously the persons who had used the Grand Rapids water the longest and who were 40–50 years or older at the time of death were the most desirable subjects for this series of studies. In epidemiologic surveys of material obtained at autopsy, however, data on the persons best qualified for the studies are often difficult to obtain.

Furthermore, we excluded persons who had chronic diseases known to affect the bone structure, such as cancer, leukemia, severe anemia, parathyroid disease, and renal disease that was severe enough to cause uremia. Persons who had had nephrosclerosis of a vascular character, a common observation in the elderly at necropsy, were included unless the condition was accompanied by renal failure. Most of the deceased in the study had a short history of illness, such as myocardial infarction, pulmonary embolism, cerebral vascular disease, pneumonia, or trauma. This selectivity restricted the number of cases in the study.

Analytical procedure. The bone specimens, cleaned of soft tissue, were cut into small pieces, weighed, and dried overnight at 100° C. The dry weight was recorded, and the specimens were extracted for 8 hours with absolute alcohol and then for 4 hours with an extraction of ether. Pulverized to an approximate 60 mesh powder, the sample was weighed into a platinum crucible and ashed at 1,030° F. overnight. Aorta specimens, freed of coagulated blood and debris, were extracted and similarly ashed.

A 17 to 33 mg. sample of the ash was dissolved in 1 ml. of 0.5M $HClO_4$; 4 ml. of 0.5M trisodium citrate were added, and fluoride content was determined with a fluoride electrode as described by McCann (*14*).

Another 14.5 to 15.5 mg. sample of ash was placed in a 25 ml. flask, dissolved in 2 ml. of 6N HCl, heated if necessary, and the solution made up to volume. Calcium was determined on a 5 ml. aliquot by first adding 5 ml. of 3 percent La in 3M $HC1O_4$ and diluting the solution to 50 ml.; the Ca content was measured on a Perkin-Elmer 303 atomic absorption spectrophotometer with an appropriate lamp.

Histopathological methods. Specimens of the anterior portions of the bodies of the lumbar vertebrae and the anterolateral ends of the left sixth or seventh ribs were studied. Also, the abdominal segment of the aorta was examined in a minority of the cases. The specimens were fixed for at least 96 hours in 10 percent formalin buffered with saline, and then the bone blocks were sawed to size and shape. The vertebral section selected for microscopic examination included the anterior portion of the intervertebral joint and the adjacent lumbar vertebral body on each side.

Next, the blocks were decalcified in a mixed formic acid and sodium citrate solution, usually for 7 to 10 days. After satisfactory decalcification, the tissue blocks were trimmed and then processed by routine histological methods, including paraffin embedding. Sections 6 microns thick were cut, and at least two slides were prepared on each specimen. One was stained with hematoxylin and eosin; the next serial section was stained with a combined Van Gieson and colloidal iron technique (*15*).

In the microscopic studies, we stressed comparative examination, and we were able to match 62 Grand Rapids residents with 62 New York controls according to age and sex. Slides of bone specimens from the two groups were then compared. An attempt was made to quantitate the normal bone structure in each group. The representative thickness of cortical and medullary trabecular bone was estimated with an ocular micrometer. Examination of matched slides from the two groups side by side in a comparison microscope afforded an overall impression of normal bone volume. The representative bone thickness in micrometer units (and the unit value in millimeters) with the deceased's age and sex was listed and subjected to a statistical test. Finally, any qualitative microscopic changes in the bones, the marrow, the intervertebral joint, the parosteal tissue, and the aorta were noted.

Besides the 62 matched pairs, observations were also made on 41 of the deceased who could not be matched by age and sex with members of the other community; 25 of these unmatched persons were from New York and 16 from Grand Rapids. The quantitative estimates of bone volume could be done only for the persons who were 41 years or older at time of death; the numbers in the younger groups were too small for statistical evaluation.

A discrepancy between the total number of specimens subjected to chemical analysis and those studied for histopathology is due to the loss of some materials in the mail.

Results

Chemical analysis. The results of chemical analysis of specimens from the two groups in our series, with the age and years of use of the local drinking water, are shown in table 1. Except for four persons in the age group 0–20 years, the fluoride levels in the vertebrae and ribs of the Grand Rapids residents were consistent (0.095–0.307 percent in the vertebrae and 0.079–0.206 percent in the rib bones) and differed significantly from levels in the New York controls. These data correspond well with previous fluoride levels in the bones associated with prolonged use of drinking water containing fluoride naturally at a level of 1.0 ppm, including previous analyses of the fluoride in bone specimens of Grand Rapids residents (*11*). The bone fluoride in the majority of the New York residents was less than 0.10 percent, a quantity consistent with the fluoride present in skeletal tissues of persons using drinking waters of low fluoride content (*11,16,17*).

Extensive data obtained by Smith on the fluoride in rib and vertebral samples of long-term residents of Rochester, N.Y., before supplemental fluoride was added to the city's drinking water, indicate a rise in bone fluoride with age (*16*). The data on our cases likewise suggest an increase of bone fluoride in older age groups, both in Grand Rapids and New York. Call and associates have published extensive similar data on the increase in bone fluoride with age in persons exposed to minimum amounts of fluoride (*17*).

The ash and calcium content of both the vertebrae and the ribs of the New York residents did not differ significantly from that of the Grand Rapids residents. The fluoride in the bones of the Grand Rapids residents was not sufficient to affect the ash and calcium content (*18*).

A constant fluoride intake over a prolonged period results in a maximal, relatively fixed concentration of fluoride in the skeletal tissue. This remarkable "plateau" concentration is evidenced in the close correlation between fluoride in drinking water and fluoride in human bones (*11,19,20*). This phenomenon has also been found in experiments with the ubiquitous white rat. Zipkin and McClure, having given rats aged 30 to 330 days equal quantities of fluoride over specified periods,

Table 1. Percentage of ash, calcium, and fluorine in vertebrae, ribs, and abdominal aortas of residents of Grand Rapids, Mich., and New York, by age at death and years of residence in community

Grand Rapids residents						New York residents					
Number	Age (years)	Years of residence	Ash	Calcium	Fluorine	Number	Age (years)	Years of residence	Ash	Calcium	Fluorine
					Specimens of vertebrae						
4	0–20		43.48	34.45	0.054	3	0–20		45.77	36.19	0.049
1	21–40	>20	47.75	36.79	.095	2	21–40	>20	45.38	35.34	.070
2	41–60	<20	48.42	36.47	.178	7	41–60	<20		35.83	.097
8	41–60	>20	48.55	36.59	.195	15	41–60	>20	46.53	35.54	.082
8	41–60	[1]	48.76	36.13	.176						
1	61–80	<20	38.45	35.80	.148	1	61–80	<20		34.50	.052
13	61–80	>20	51.32	37.00	.195	17	61–80	>20	45.76	35.06	.087
8	61–80	[1]	45.75	35.71	.242						
2	>80	<20	45.18	36.73	.195	4	>80	<20		38.51	.103
7	>80	>20	47.23	36.64	.307	10	>80	>20	44.61	35.92	.121
5	>80	[1]	46.87	34.66	.294						
					Specimens of ribs						
4	0–20		54.80	35.92	0.040	3	0–20		56.18	36.90	0.042
1	21–40	>20	53.21	29.03	.206	5	21–40	>20	54.29	35.30	.054
2	41–60	<20	57.55	36.08	.107	14	41–60	>20	55.81	35.64	.065
8	41–60	>20	59.08	37.17	.124						
8	41–60	[1]	55.70	36.78	.134						
1	61–80	<20	53.77	36.28	.079	1	61–80	>20	56.85	35.45	.038
13	61–80	>20	53.83	35.18	.188	17	61–80	<20	55.09	34.38	.076
8	61–80	[1]	52.06	35.13	.198						
2	>80	<20	52.84	37.15	.159						
8	>80	>20	54.60	37.40	.186	9	>80	>20	53.86	34.72	.120
4	>80	[1]	54.85	36.33	.187						
					Specimens of abdominal aortas						
1	0–20		3.58	13.44	0.021	1	0–20		5.05	15.05	0.234
1	21–40	>20	3.08	16.08	.029	2	21–40	>20	2.46	25.68	.066
2	41–60	<20	9.26	25.59	.84	6	41–60	>20	23.99	24.30	.035
8	41–60	>20	15.01	26.77	.137						
8	41–60	[1]	9.03	16.49	.104						
1	61–80	<20	13.19	33.59	.086	8	61–80	>20	22.47	23.10	.089
11	61–80	>20	21.45	28.57	.153						
8	61–80	[1]	25.81	30.17	.205						
2	>80	<20	13.01	22.75	.136	2	>80	>20	35.55	34.78	.155
7	>80	>20	24.42	32.56	.246						
4	>80	[1]	31.32	34.86	.162						

[1] Undetermined.

NOTE: The total number of specimens subjected to chemical analysis was smaller than the total number studied for histopathology because some materials were lost in the mail.

demonstrated that, as the rats aged, there was a striking reduction in their capacity to acquire fluoride in their bones and teeth (*21*).

Analytical data on the abdominal aorta of the New York residents are limited (table 1). The aorta specimens of the Grand Rapids residents (excepting two persons in the age group 41–60 years) showed an average of approximately 0.15 percent (0.021–0.246 percent) of fluoride. Call and associates (*17*) have published data on fluoride in the aorta indicating an average of 0.0018 percent present. Smith and co-workers (*22*) reported a significantly higher percentage of fluoride in the aorta than in other soft tissues. The accumulation of radioactive fluorine at local sites of calcification has been demonstrated by Ericsson and Ullberg (*23*) in their extensive survey of fluoride in soft tissues. The known propensity of aortic and other soft tissue to calcify may account for the increased concentration of fluoride in such tissue.

Histopathology. Sixty-two matched pairs from Grand Rapids and New York showed no consistent differences in quantitative bone structure when observed under the comparison microscope (table 2). In 18 patients from Grand Rapids, the spongy medullary bone in the vertebrae was somewhat thicker than in the New York controls; in 12 pairs, it was thicker in the controls; in 32 pairs, the bone structure of the vertebral medulla was similar. When the estimated numerical values were subjected to statistical testing, no significant difference could be found between the values for the vertebral medulla in the two series (tables 3 and 4). The rib cortex of the Grand Rapids women in the age group 61–80 years did seem to be thicker than in the controls (table 4). This impression, however, could not be supported in any other female age group or in any of the male age groups listed in table 3.

Twelve patients from Grand Rapids and 12 patients of similar age from New York were compared, with special attention to the fluoride content of their bones (table 5). These 24 patients represented the range of fluoride levels as determined chemically. The microscopic measurements of bone thickness are also listed in table 5 to indicate any correlation between high and low chemical values.

The fluoride levels in the bones of the Grand Rapids residents varied from 0.090 to 0.33 percent. Only in patient 66–1092, was a correlation found between the fluoride level and a change in bone thickness. The rib cortex of this patient was thicker than the rib cortex of most patients in the 41–80 years age group, and the patient's fluoride level was the highest of the range. Patient 66–923, who had the lowest percentage of fluoride, had somewhat thicker vertebral and rib medullary bone than patient 66–1092. Patient 67–1110, who had the lowest fluoride level in either series (table 5), had a bone structure similar tó that of patient 66–1092.

In older patients, similar com-

Table 2. Results of comparison of quantitative normal bone structure of the 62 matched pairs at four sites

Site	Number of pairs with bone structure— Similar	Thicker in Grand Rapids resident	Thicker in New York control
Vertebral cortex	43	10	9
Vertebral medulla	32	18	12
Rib cortex	20	21	21
Rib medulla	40	12	10

Table 3. Quantitative estimates of bone thickness in vertebral cortex and medulla and in rib cortex and medulla of male residents of Grand Rapids and New York, by age group

	Grand Rapids residents				New York residents			
	Vertebra		Rib		Vertebra		Rib	
	Cortex	Medulla	Cortex	Medulla	Cortex	Medulla	Cortex	Medulla
	41–60 years[1]							
	2.5	2.5	5.0	2.0	2.5	2.0	5.0	1.5
	3.0	2.0	7.0	1.5	3.0	2.5	6.0	1.5
	3.0	2.5	15.0	2.5	2.0	2.5	6.0	1.5
	2.5	3.0	12.0	1.5	2.5	2.0	10.0	1.0
	3.0	2.5	6.0	2.0	3.0	2.5	9.0	2.0
	3.0	2.0	10.0	1.5	3.0	2.0	10.0	2.0
	3.0	1.5	5.0	1.5	3.0	2.0	5.0	1.5
	3.0	2.0	10.0	1.5	3.0	2.0	9.0	1.5
	3.0	2.5	16.0	2.0	2.0	1.5	7.0	1.5
	3.0	2.5	10.0	1.5	3.0	2.5	10.0	1.5
Mean	2.9	2.27	9.55	1.77	2.7	2.15	7.44	1.55
S.D.	.20	.45	4.16	.37	.41	.33	2.07	.31
S.E.	.06	.15	1.38	.12	.12	.10	.69	.10
t test	1.42	.94	1.37	1.57				
	61–80 years							
	2.0	2.5	5.0	2.0	2.0	2.5	5.0	2.5
	4.0	3.0	6.0	2.0	2.0	1.5	10.0	2.0
	3.0	2.0	8.0	1.5	5.0	2.0	12.0	1.5
	2.5	2.0	6.0	1.5	2.5	1.5	8.0	1.5
	3.0	2.5	11.0	2.5	3.0	2.5	9.0	2.5
	3.0	1.5	9.0	1.5	3.0	2.0	7.0	1.5
	2.0	1.5	7.0	1.5	3.0	2.5	10.0	2.5
	4.0	2.5	3.0	1.5	4.0	2.0	8.0	1.5
	4.0	2.0	10.0	1.5	2.5	2.0	8.0	1.5
	3.0	2.0	6.0	2.0	3.0	2.0	6.0	1.5
	4.0	1.5	6.0	1.5	4.0	2.5	6.0	1.5
Mean	3.05	2.15	7.10	1.75	3.00	2.05	8.30	1.85
S.D.	.76	.46	2.42	.34	.91	.36	2.05	.46
S.E.	.24	.14	.76	.10	.28	.11	.64	.14
t test	.13	.58	1.20	.58				
	Over 80 years							
	2.5	2.0	5.0	1.5	2.5	2.0	5.0	1.5
	3.0	3.0	12.0	2.0	3.0	3.0	7.0	1.5
	3.0	2.5	9.0	1.5	5.0	1.5	9.0	1.5
	2.5	2.0	8.0	1.5	2.5	2.0	8.0	1.5
	3.0	2.5	8.0	2.0	2.0	2.5	9.0	2.0
	4.0	2.5	8.0	2.5	4.0	2.0	6.0	1.5
Mean	2.80	2.40	8.40	1.70	3.00	2.20	7.60	1.60
S.D.	.26	.41	2.50	.26	1.17	.56	1.67	.22
S.E.	.11	.18	1.12	.11	.52	.25	.74	.09
t test	.37	.64	.59	.71				

[1]There were insufficient numbers for statistical analysis in the age groups 0–20 and 21–40 years.

NOTE: Each value is an estimate of representative thickness by oculomicrometer measurement. Unit value is 0.05 mm.

parisons between the patients with the lowest and highest fluoride percentages (patients 66–925 and 66–1101) also failed to show any consistent correlation of bone fluoride levels with bone structure (table 5).

Moreover, qualitative changes in bone structure could not be correlated with the fluoride content of the bones. In patient 66–739, a control, focal subacute periostitis was observed in the section of lumbar vertebra (table 5). The only other histopathological observation on the patients listed in table 5 was focal muscular atrophy adjacent to the rib in patient 66–1101.

Other qualitative changes noted in both groups were increased focal osteoclasia, which was observed in the bones of 14 Grand Rapids residents and in five New York controls. Nonspecific subacute periostitis was also observed in the bones of one Grand Rapids resident and of four New York controls, including patient 66–739. Focal cartilaginous metaplasia was noted in one bone of a patient from each group. Amyloid deposits were observed in the vertebral periosteum of one Grand Rapids patient and in none of the controls. Focal irregular hyperplasia, suggestive of old Paget's disease, was seen in the vertebral medulla of one New York control. This change was not encountered in the Grand Rapids residents.

The bone marrow of both groups showed focal eosinophilia and myeloid hyperplasia of equal frequency and degree. Similarly, occasional lymph follicles were observed in the bone marrow of both groups. Focal sarcoidosis was encountered only in the marrow of one New York control. One Grand Rapids patient only showed active focal tuberculosis

Table 4. Quantitative estimates of bone thickness in vertebral cortex and medulla and in rib cortex and medulla of female residents of Grand Rapids and New York, by age group

	Grand Rapids residents				New York residents			
	Vertebra		Rib		Vertebra		Rib	
	Cortex	Medulla	Cortex	Medulla	Cortex	Medulla	Cortex	Medulla
	41–60 years [1]							
	2.0	1.5	10.0	1.0	2.0	1.5	12.0	1.5
	5.0	3.0	10.0	1.5	3.0	2.0	6.0	2.0
	2.5	2.0	11.0	2.0	3.0	2.0	6.0	2.0
	3.0	2.0	8.0	1.5	4.0	2.0	9.0	2.0
	3.0	2.0	4.0	1.5	3.0	1.5	13.0	1.5
	3.0	2.0	8.0	2.0	3.5	2.5	11.0	2.0
Mean....	3.10	2.10	8.60	1.50	3.00	1.80	9.20	1.80
S.D.....	1.14	.54	2.79	.34	.70	.26	3.27	.26
S.E......	.51	.24	1.25	.15	.31	.11	1.46	.11
t test....	.16	1.15	.31	1.50	....	....	....	....
	61–80 years							
	2.5	2.5	6.0	2.0	3,0	2.5	7.0	1.5
	1.5	1.5	5.0	2.0	2.5	2.0	5.0	2.0
	3.0	2.0	8.0	2.0	3.0	2.0	4.0	1.5
	3.0	2.0	4.0	1.5	4.0	2.0	7.0	1.5
	4.0	2.0	8.4	1.5	4.0	3.0	6.0	1.5
	3.0	1.5	6.0	1.5	3.0	2.0	6.0	1.5
	3.0	2.0	8.0	2.0	6.0	2.0	5.0	1.5
	3.0	2.0	7.0	2.0	3.0	2.0	3.0	2.0
	3.0	2.5	6.0	2.5	3.0	2.0	3.0	2.0
	3.0	2.0	3.0	1.5	3.0	2.5	6.0	2.5
	3.0	2.0	10.0	2.0	3.0	1.5	6.0	1.5
	3.0	3.0	12.0	1.5	3.0	2.5	6.0	1.5
	3.0	2.0	10.0	1.5	3.0	2.0	4.0	1.5
	....	....	....	....	3.0	2.0	8.0	1.5
Mean....	2.91	2.08	6.91	1.83	3.34	2.15	5.23	1.69
S.D.....	.57	.42	2.51	.33	.91	.38	1.36	.33
S.E......	.16	.12	.72	.09	.25	.10	.37	.09
t test....	1.43	.50	2.10	1.40	....	....	....	....
	Over 80 years							
	2.5	2.0	5.0	1.5	2.5	2.0	5.0	1.5
	4.0	3.0	5.0	2.0	3.0	3.0	5.0	2.0
	2.0	1.5	10.0	1.5	2.0	1.5	10.0	2.0
	3.0	2.5	6.0	2.0	3.0	2.5	8.0	2.0
	4.0	2.0	4.0	2.0	1.5	2.5	4.0	2.5
	3.0	2.0	5.0	1.5	3.0	2.0	6.0	1.5
	3.0	2.0	6.0	2.0	3.0	1.5	9.0	2.0
	3.0	2.0	5.0	2.0	3.0	2.0	5.0	1.5
	3.0	2.5	5.0	2.0	....	....	....	....
Mean....	3.06	2.12	5.75	1.81	2.57	2.14	6.71	1.92
S.D.....	.67	.44	1.83	.26	.60	.55	2.29	.36
S.E......	.23	.15	.64	.09	.22	.20	.86	.13
t test....	1.48	.07	.89	.78	....	....	....	....

[1] See footnote 1, table 3.

NOTE: Each value is an estimate of representative thickness by oculomicrometer measurement. Unit value is 0.05 mm.

in the bone marrow. In two New York controls, only focal bacteremia was found in the marrow. Also, the marrow of one control only revealed depressed hematopoiesis.

Vertebral osteoarthritis was most often manifested by bone "spurs" or "lips." Such osteophytes were sometimes accompanied by haphazard mixtures of bone, fibrous tissue, and cartilage near their point of attachment and close to the junction of hyaline articular cartilage and cortical bony plate. Associated observations in the annulus fibrosus included fibrillation, irregular porosity, and capillary proliferation. In 39 matched pairs, vertebral osteoarthritis, as defined earlier, was absent or present in the same degree. In 14 New York controls, it was more severe than in the matched residents of Grand Rapids and in nine pairs the reverse was true.

Abdominal aortic atherosclerosis was studied microscopically and chemically in 20 New York controls and 69 Grand Rapids residents. In the controls, the changes were graded histopathologically as mild in five, moderate in six, and severe in nine. In the patients in the Grand Rapids series, these changes were evaluated as mild in eight, moderate in 22, and severe in 39.

Table 5. Correlation of chemical values for bones of Grand Rapids and New York residents 41–80 years old at death with microscopic bone structure and exposure to fluoride

Grand Rapids residents' age group and case number	Calcium	Fluorine	Years exposure to fluoride	Microscopic bone thickness [1]			
				Vertebra		Rib	
				Cortex	Medulla	Cortex	Medulla
41–60 years:							
67-1038.	34.85	0.176	Unknown	3.5	1.5	10.0	2.0
66-519..	35.68	.211	>25	2.0	1.5	10.0	1.0
66-386..	37.70	.115	25	2.5	2.5	5.0	2.0
66-1106.	35.80	.200	12	2.5	2.0	11.0	2.0
66-923..	36.55	.090	Unknown	3.0	2.5	6.0	2.0
66-1092.	37.28	.337	>25	3.0	2.0	10.0	1.5
61–80 years:							
67-1035.	33.06	.211	Unknown	3.0	2.0	6.0	2.0
66-1102.	38.32	.112	>25	4.0	2.5	3.0	1.5
66-925..	37.60	.106	>25	3.0	1.5	6.0	1.5
66-529..	38.11	.178	>25	2.5	2.0	6.0	1.5
66-527..	33.89	.154	>25	3.0	2.0	8.0	1.5
66-1101.	37.12	.313	Unknown	2.0	1.5	[2] 7.0	1.5

[1] Each value is an estimate of representative thickness by oculomicrometer measurement. Unit value is 0.05 mm.
[2] Parosteal focal muscle atrophy.

Discussion

Before we obtained these data on skeletal fluoride from Grand Rapids, studies by Zipkin and co-workers had related human skeletal fluoride (F) to the quantity of fluoride in the drinking water (*11*). They analyzed bone specimens taken at autopsy from Grand Rapids (1.0 ppm F), Colorado Springs (2.5 ppm F), Amarillo, Tex. (2.8 ppm F), and Lubbock, Tex. (4.0 ppm F). There was a remarkably close correlation between the percentage of fluoride in the bones and the parts per million of fluoride in the subjects' drinking water.

According to the previous data, five Grand Rapids residents who had ingested the water of that city (1.0 ppm F) not longer than 12 years and whose average age when they started to use the fluoridated water was about 63 years showed a mean concentration of 0.146 percent of fluoride in their relatively old bones (*11*). The data on skeletal fluoride in our report support these previous limited analytical data from Grand Rapids.

In general, the bone structure in the two groups we studied showed no significant difference, quantitatively. A greater incidence of increased focal osteoclasia was observed in the Grand Rapids series, but the great majority of bones in both groups did not demonstrate such a change. This condition was observed in 19 bone specimens from Grand Rapids and five of the New York control specimens. In a previous study, the difference in osteoclasia was insignificant when bones of patients residing in areas with low fluoride levels in the drinking water were compared with bones of those residing in areas with high levels (*12*).

Vertebral osteoarthritis seemed to be more frequent in the New York controls.

The incidence and severity of abdominal aortic atherosclerosis were approximately alike in the two groups. Both osteoarthritis and abdominal aortic atherosclerosis were believed to be incidental to aging and unrelated to fluoride ingestion.

Conclusions

The bone specimens of the Grand Rapids residents contained a quantity of fluoride concomitant with prolonged use of water containing one part per million of fluoride. These results furthermore demonstrate that mature bones can acquire fluoride and that the quantity will remain at a relatively steady "plateau" of concentration.

A comparative microscopic examination of the vertebrae and ribs from patients in two series, one from areas with low fluoride in the drinking water and the other from Grand Rapids with artificially fluoridated drinking water, showed no consistent differences.

In the light of these data and epidemiologic studies of the effects on the skeleton of drinking waters of relatively high fluoride content, the quantity of fluoride in the Grand Rapids bone specimens does not appear sufficient

Table 5. Correlation of chemical values for bones of Grand Rapids and New York residents 41–80 years old at death with microscopic bone structure and exposure to fluoride—Continued

New York residents' age group and case number	Calcium	Fluorine	Years exposure to fluoride	Microscopic bone thickness [1]			
				Vertebra		Rib	
				Cortex	Medulla	Cortex	Medulla
41-60 years:							
66-739..	34.86	0.036	0	[3] 3.0	2.5	9.0	2.0
67-846..	36.55	.116	0	3.0	2.0	5.0	1.5
67-1110.	34.98	.032	0	3.0	2.5	10.0	1.5
66-552..	37.18	.066	0	2.5	3.0	8.0	1.5
66-387..	35.59	.046	0	3.0	2.5	6.0	1.5
66-516..	35.94	.133	0	2.0	2.5	6.0	1.5
61-80 years:							
66-524..	33.59	.057	0	4.0	2.0	7.0	1.5
67-1113.	34.95	.054	0	4.0	2.5	6.0	1.5
66-512..	34.42	.021	0	2.5	2.0	5.0	2.0
67-1109.	36.73	.083	0	4.0	2.0	10.0	1.5
66-526..	34.52	.084	0	2.0	1.5	10.0	2.0
66-752..	34.33	.172	0	3.0	2.0	6.0	1.5

[3] Focal subacute periostitis.

to have exerted a beneficial effect on patients with bone disease such as osteoporosis.

In addition to the bone specimens, the lumbar intervertebral body joints and the abdominal aorta were studied comparatively. They showed microscopic changes incidental to aging with approximately equal frequency in both series. Intervertebral osteoarthritis and aortic atherosclerosis seemed to be unrelated to fluoride intake.

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Data were obtained on the quantity of fluoride in the bones of deceased residents of Grand Rapids, Mich., and on the microscopic structure of those tissues after prolonged consumption by the residents of the city's fluoridated water. Grand Rapids recently has completed 20 years of fluoridation at a level of 1.0 ppm. These data on Grand Rapids were then compared with those on deceased residents of two control cities in New York State, New York and Albany, where fluoride in the drinking water was of the order of 0.1 ppm or less. The data on deceased residents of New York City were obtained before that city instituted artificial fluoridation in 1965.

The bone specimens of the Grand Rapids patients contained a greater quantity of fluoride than the controls. The results demonstrate that the fluoride acquired by mature bones will remain at a relatively steady "plateau" of concentration. Comparative microscopic examination of bones in the two series showed no consistent differences. There was no evidence that prolonged consumption of the Grand Rapids fluoridated water had any adverse effects on skeletal structure. The quantity of fluoride in the Grand Rapids bone specimens does not appear to have been sufficient to exert a beneficial effect on patients with osteoporosis.

Others Assisting in the Study

The material from Grand Rapids was made available by Dr. J. D. Mann, Dr. D. L. Kessler, Dr. C. A. Payne, Dr. H. E. Bowman, R. E. Flexman, and H. E. Samuelson. Dr. W. A. Thomas, Dr. E. Panlilio, and Dr. E. Anzola provided the material from Albany. Dr. Finn Brudenvold assisted in the bone analysis at the Forsyth Dental Center in Boston.