Effect of Fluoride In Drinking Water

on the osseous development of the hand and wrist in children

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NUMEROUS CLINICAL, as well as experimental, studies have produced evidence that detrimental effects on skeletal tissues may result from prolonged exposure to large quantities of fluorides. Roholm (*1*) described the skeletal effects of an estimated exposure amounting to 25 to 30 mg. fluorine (F) inhaled daily for 9 years or longer as follows: "The pathological process may be characterized as a diffuse osteosclerosis in which the pathological formation of bone starts both in periosteum and in endosteum; compacta densifies and thickens; the spongiosa trabeculae thicken and fuse together. The medullary cavity decreases in diameter. There is considerable new formation of bone from periosteum, and ligaments that normally do not calcify, or only advance in age, undergo a considerable degree of calcification." Exposure to cryolite dust was the cause of the bone pathology observed by Roholm, as it was of that reported by Moller and Gudjonsson (*2*).

Dr. McCauley, now director of the bureau of dental care of the Baltimore City Health Department, was engaged in research on problems related to dental health at the National Institute of Dental Research, National Institutes of Health, Public Health Service, from 1945 to 1949. Dr. McClure is chief of the Laboratory of Oral and Biological Chemistry, National Institute of Dental Research. Associated with the National Institutes of Health since 1936, Dr. McClure has done extensive research on the physiological effects of fluorine.

Prolonged exposure to fluoride in quantities over 10 p.p.m. F in drinking water has been reported responsible for chronic fluorosis characterized by rigidity in the spine, stiffness, and immobility of the joints, symptoms similar to those recorded by Roholm. These effects, attributed to excessive waterborne fluoride, have been observed endemically in the Madras Presidency (*3*) and the Punjab (*4*) of India and in the Pretoria district (*5*) of South Africa. As pointed out by McClure (*6*), not only is the fluoride content of the drinking water excessive in these areas, but also the hot climate increases water consumption, and low dietary and other living standards possibly aggravate the manifestations of skeletal abnormalities.

Exposure in the United States

In the United States, about 4.5 percent of the population is now using water which naturally contains 0.5 to 8.0 p.p.m. F. In addition, approximately 785 communities with a total population of about 15.5 million are (November 1953) using water supplies in which the fluoride level is maintained within the range 0.7 to 1.5 p.p.m. F, by controlled fluoridation, for the reduction of dental caries. In excess of 1.5 p.p.m. F in drinking water, fluoride is responsible for the production of endemic dental fluorosis, or mottled enamel, in varying degrees of severity and incidence (*7*).

A reliable basis for the point of view that concentrations of fluoride in drinking water up to 1.5 p.p.m. are not a public health hazard is the evidence pertaining to urinary excretion. When the drinking water contains as much as 4.5 p.p.m. F, excretion is more than 90 percent effective (*6*, *8*, *9*). Such a highly efficient excretion largely negates the possibility of cumulative skeletal fluorosis from continuous exposure to drinking waters containing up to 4.5 p.p.m. F.

Further evidence of the harmlessness of low-fluoride water is available in observations relating specifically to the skeletal tissues. McClure (*10*) found that exposure to fluoride waters containing up to 4.5 p.p.m. F affected neither the bone-fracture experience nor the height and weight of high school boys and young men. A skeletal survey (*11*) of children and adults living in an area of endemic mottled enamel and exposed to drinking water containing 1.5 to 3.0 p.p.m. F yielded no radiological evidence of bone abnormality. Smith (*12*) also reported no changes in calcium and phosphorus metabolism in children with mottled enamel.

Indications that the fluorine concentration of the skeletal tissues increases gradually with age were found in an analysis of the ribs and vertebras of 158 persons with continuous lifelong residence in an area of relatively fluoride-free domestic water (*13*). It is probable that the fluorine in skeletal tissues can increase several times above average quantities without causing a deleterious skeletal effect (*6*).

In a comparison of medical histories and results of physical examinations, including complete X-rays, on adults who had lived 15 years or longer in Bartlett, Tex., where the drinking water contained 8.0 p.p.m. F, with similar information on adults living in Cameron, Tex., where the drinking water contained about 0.3 p.p.m. F, the only difference in the health status was shown by the X-rays. Among the Bartlett adults, 12 percent, all of whom were over 50 years of age and had used the Bartlett drinking water for more than 35 years, showed a somewhat coarser trabecular structure of the bones. These bone changes produced no effective signs or subjective symptoms related to the skeletal system and were regarded as having no general health significance (*14*).

The present study was organized to provide additional data on the skeletal effects of exposure to fluoride in drinking water in the United States. It was designed to determine specifically the effects of continuous exposure to drinking water containing 3.5 to 5.5 p.p.m. F on ossification and skeletal maturation as indicated by radiographs of the hand and wrist of children 7 through 14 years old.

Radiographic Studies of Bone Development

Because it is accessible and relatively convenient to radiograph, the hand has been the subject of frequent X-ray study since Roentgen's discovery. Ranke (*15*) in 1896, using wrist films, was apparently the first to witness skeletal growth. Pryor (*16*) in 1905 reported the earliest extensive roentgen-ray observations of bone growth and development in the hand.

Pryor (*16,17*) studied more than 500 films of children from birth to 14 years of age and found a definite and uniform order of ossification of the carpal bones. Although the centers of calcification practically always appeared in the same order, the progress of ossification was subject to delay by ill health, metabolic disorder, interference with blood supply, accident, or disease. He discovered also that the skeleton of the growing girl is more mature than that of the boy of the same age and that the hand is a good index of ossification of the entire skeleton (*18*).

Skeletal Age

Comprehensive investigations by Flory (*19*), Todd (*20*), Greulich (*21*), and others have, in general, confirmed and amplified the observations of the early investigators and provided standards for the practical assessment of skeletal age by radiographic inspection of the hand. Ample evidence that the progress of development of the bones of the hand and wrist parallels that of the rest of the skeleton is provided in these and numerous other reports of the chronology of appearance and fusion of centers of ossification throughout the body. Todd (*20*) assessed skeletal maturity on the basis of X-ray findings in the hand, foot, elbow, knee, shoulder, and hip and decided that the hand was the most reliable single index.

The standards used to assess skeletal age in the present study are the composite record of skeletal development of Cleveland children from all grades of society, except the destitute, without regard to ethnic origin, stature, or weight (*20*). They represent large numbers of children radiographed at 6-month age intervals from birth through the 18th year and have been widely utilized in overall growth studies.

Ossification Index

Use of skeletal age in attempts to grade children for educational purposes caused investigators to seek a procedure for determining developmental status more objective than the inspectional technique. Baldwin (*22*) in 1921 was the first to report measurement of the carpal bones for this purpose, using a planimeter to ascertain the total area of their shadows on the X-ray picture. Later, Baldwin, Busby, and Garside (*23*) published a series of such measurements for school-age children, corrected for gross size by dividing the ossified area by the area of a rectangle of dimensions derived from two diameters of the wrist obtained with calipers. Similar quantitative indexes and norms of skeletal development were produced by Carter (*24*) and Kelly (*25*). The Carter (*24*) method, used in the present study, has been applied successfully in general growth (*19*) and nutritional (*26*, *27*) problems in children.

Study Areas

Amarillo and Lubbock, in western Texas, were selected for this study because they are the two largest communities in the United States having 3.5 p.p.m. F or more in their public water supplies. The populations are 74,000 and 71,000, respectively.

The fluoride content of the drinking water in Amarillo, according to frequent analyses by the city chemist, ranged from 3.6 p.p.m. F to 6.2 p.p.m. F during the period 1934 through 1948. The study was made in 1948. Monthly analyses by Elvove (*28*) in 1933 and 1934 averaged 3.9 p.p.m. F. In 1948, McClure found 3.3 p.p.m. F in a single sample of water. The water supply in Lubbock has been more constant in fluoride content. In 1933 and 1934, it averaged 4.4 p.p.m. F (*28*); in 1943, 3.8 p.p.m. F (*8*); and in 1948, 3.5 p.p.m. F. The epidemiological data on the distribution of mottled enamel in these two communities reported by Dean (*7*) are in agreement with these analyses (see table 1).

Water supplies in the Texas Panhandle generally contain from 2.0 to 5.0 p.p.m. F (*7*). Anyone living in Amarillo or Lubbock or in their wide environs would be exposed to fluoride drinking water.

Cumberland, in western Maryland, was selected as the control city. Its population is 37,000, and its water supply is obtained by impounding surface water flowing in a nearby mountain stream. At the time of the study, the water contained 0.12 p.p.m. F. This low level of waterborne fluoride produces no mottled enamel in the Cumberland population.

Table 1. Percentages of school children in Amarillo and Lubbock, Tex., affected by mottled enamel [1]

Community	Signs absent		White opaque spots		Brown stains and pitting	
	Normal	Questionable	Very mild	Mild	Moderate	Severe
Amarillo, Tex.	3. 1	6. 6	15. 2	28. 0	33. 9	13. 2
Lubbock, Tex.	1. 1	1. 1	12. 2	21. 7	46. 0	17. 9

[1] Data from reference 7.

Study Procedures

Children selected for radiography had histories of continuous residence in the communities and continuous consumption of the local drinking water. This information was obtained by means of a questionnaire completed and signed by parents. No child with a history of absence from his community for more than 6 months at one time was included in the survey. Children aged 7 through 14 years were selected because they were accessible in the public schools and because this age span covers a period of rapid calcification and growth of the bones of the hand and wrist.

Mottled Enamel Diagnosis

While the children of Amarillo and Lubbock were at hand for their X-ray photographs, their teeth were inspected for mottled enamel. A record was made of the degree of mottling observed, using a simple comparative score of none, mild, moderate, or severe. The presence of moderate or severe mottled enamel is evidence of continuous exposure to fluoride drinking water during the period of tooth formation. Mild mottling or the absence of mottling may be attributed to reduced susceptibility to fluorine or to a reduced consumption of the local water supply during formative tooth life.

Radiographs

An X-ray picture showing the right hand and wrist of each child in the study was made in the school using portable equipment and a standard technique (*19*). This radiograph was produced on 5-inch x 7-inch no-screen film in a cardboard holder with 10 milliampere-seconds exposure, 70 peak kilovolts output, and 32-inch target-film distance. It was identified by a serial number applied with lead numerals on exposure, corresponding to the number assigned to the questionnaire returned by the child's parent. For densitometric purposes, an ivory step tablet was included in each exposure. Most of the films were developed in the field, usually on the day they were exposed. Radiographs of 2,050 children—965 boys and 1,085 girls—were used in the study. Distribution of the children by age and community of continuous residence is given in table 2.

Ossification Index

The films were used to establish a quantitative index of skeletal development for each child, employing the technique of Carter (*24*). According to this method, the areas of the shadows of the eight carpal bones and of the radial and ulnar epiphyses are measured with a polar planimeter. Their sum, the total ossified area, is divided by the area of a quadrilateral anatomically described for each film. The quotient is the ossification ratio. This ratio is an index of carpal ossification of the child, subject of the radiograph, corrected for his size, and therefore comparable to like indexes derived for other children. It reflects the status of development of the skeleton as a whole and may be correlated with chronological age in normally growing children.

In a test of reliability, the ossification ratio was determined from each of 50 radiographs by McCauley. Later, without the knowledge of

Table 2. Distribution of children studied, by age, sex, and community of continuous residence

Age last birthday (years)	Amarillo, Tex.		Lubbock, Tex.		Cumberland, Md.	
	Boys	Girls	Boys	Girls	Boys	Girls
7	16	27	32	38	41	40
8	44	56	46	44	48	46
9	45	64	47	48	48	60
10	29	46	37	51	54	63
11	37	27	42	30	62	44
12	39	34	43	52	47	51
13	36	39	47	56	32	47
14	21	31	36	41	36	50
All ages	267	324	330	360	368	401

indexes previously obtained, a laboratory assistant repeated the planimetry and calculation of the ossification ratio from the same films. The second determinations were correlated with the first by coefficient 0.975. This index was similarly reliable in the hands of Flory (*19*).

Skeletal Age Rating

The same films were used to obtain a skeletal age rating for each child. This rating is a qualitative evaluation of osseous development arrived at by comparison of the child's radiograph with a series of radiographs of the hand representing standards of maturation at varying levels of chronological age. Individual films, and therefore children, were assigned a developmental age.

For purposes of this study, skeletal age was determined by observation of (*a*) the contours of the metacarpal and phalangeal epiphyses, (*b*) the progress of their union with the diaphyses, (*c*) the presence or absence of each of the eight carpal bones and of the distal epiphyses of the radius and ulna, and (*d*) their morphology and stage of diaphyseal union. The assigned rating was that of the standard radiograph in which the above determinants of maturity most nearly approached those observed in the film being rated. This method, described originally by Todd (*20*) and more recently by Greulich and Pyle (*21*), supplements the quantitative method of Carter and offers a convenient control.

The standard radiographs used in the present study were obtained from the Brush Foundation. They were selected by Todd and his coworkers from radiographs of Cleveland children included in their extensive investigations at the Western Reserve University. Two series were employed, one for boys and another for girls. In the ages 7 through 14, each series contained a standard of osseous development in the hand at 6-month intervals. Similar standards are available in the publications of Flory (*19*), Todd (*20*) and Greulich (*21*).

All assessments of skeletal age were made by McCauley. However, to test the reliability of the method, 67 radiographs each received an additional independent rating by one or another of three fellow laboratory workers. The duplicate ratings were correlated with the original by the coefficient 0.906. Flory (*19*) reported skeletal age ratings 87 to 97 percent reliable, depending on the training of the worker and the care with which the determinations are made. Todd (*20*) found that assessment of skeletal maturity from the hand was accurate to 6 months and associated with a reliability coefficient of 0.9.

Age Groupings

To provide the maximum numerical base for determining mean age-specific ossification indexes and skeletal age ratings, the films of all the children in the study were separated by sex, then listed in the order of age at the time the radiographs were exposed. The radiographs were then divided into seven overlapping yearly age groups with average ages 96, 108, 120, 132, 144, 156, and 168 months, or 8 through 14 years. Each group consisted of children whose ages did not differ from the group average by more than 6 months. For instance, a group appearing in the tables of this report as having an average chronological age of 96 months (8 years) is composed of children 7 and 8 years old on their last birthday, consistent with the 96-month mean. Similarly, the group of average age 108 months (9 years) includes children 8 and 9 years old, and the group of average age 10 consists of 9- and 10-year olds.

Results

Mean carpal ossification indexes and skeletal age ratings, together with their standard errors, for boys and girls in the age groups described above are given in tables 3 and 4. Excluding standard errors, these data are presented graphically in figures 1 through 4. Weighted mean ossification indexes and skeletal age ratings for the groups combined for all ages and for mottled enamel experience are presented in figure 5. These tables and graphs also include data obtained by Flory (*19*) for University of Chicago normal children which are suitable for comparison with the data from this study. Uniformity of the data for individual children and among the groups is apparent in the standard errors of means of the

Table 3. Mean ossification ratios, and their standard errors, of carpal bones of normal children and of children exposed and not exposed to high-fluoride waters

Average chronological age (months)	Fluoride water (3.5–4.5 p.p.m. F) Lubbock, Tex.		Fluoride water (3.3–6.2 p.p.m. F) Amarillo, Tex.		Mottled enamel, moderate or severe, Lubbock and Amarillo, Tex.	
	Number of children	Mean ossification ratio	Number of children	Mean ossification ratio	Number of children	Mean ossification ratio
Boys						
96	69	46. 62±1. 08	42	48. 94±1. 71	53	49. 29±1. 39
108	93	53. 24±1. 07	89	55. 87±1. 19	116	55. 11±0. 99
120	79	60. 34±1. 11	62	61. 73±1. 08	111	61. 05±0. 89
132	79	68. 73±1. 18	66	70. 69±1. 52	110	69. 03±0. 95
144	85	77. 54±1. 38	75	79. 51±1. 31	122	77. 78±1. 07
156	90	85. 22±1. 42	69	89. 13±1. 40	118	86. 68±1. 17
168	70	94. 42±1. 30	38	99. 29±1. 60	87	94. 87±1. 23
Girls						
96	75	58. 55±1. 21	61	61. 24±1. 28	67	60. 58±1. 32
108	90	66. 65±1. 26	120	71. 16±1. 12	130	69. 41±1. 05
120	99	76. 27±1. 17	94	82. 00±1. 28	133	79. 02±1. 03
132	63	86. 29±1. 42	59	92. 59±1. 48	92	89. 42±1. 31
144	78	95. 22±1. 02	57	99. 85±1. 05	90	97. 36±0. 90
156	108	101. 91±0. 80	72	104. 27±0. 80	135	103. 25±0. 65
168	86	107. 04±0. 61	56	109. 13±0. 92	99	107. 95±0. 59

Average chronological age (months)	Mottled enamel, zero or mild, Lubbock and Amarillo, Tex.		Nonfluoride water, no mottled enamel, Cumberland, Md.		University of Chicago normal children	
	Number of children	Mean ossification ratio	Number of children	Mean ossification ratio	Number of children	Mean ossification ratio
Boys						
96	33	45. 71±2. 02	81	47. 79±1. 13	100	52. 46±0. 90
108	54	52. 41±1. 54	96	54. 99±1. 19	100	60. 12±0. 86
120	25	61. 24±2. 02	99	61. 79±1. 14	100	68. 89±0. 96
132	27	70. 50±2. 47	116	69. 38±1. 09	100	75. 82±0. 99
144	33	80. 86±2. 31	99	80. 93±1. 20	100	84. 57±1. 01
156	33	91. 25±1. 80	67	89. 73±1. 61	100	95. 43±0. 87
168	23	99. 33±2. 23	67	98. 79±1. 31	100	101. 17±0. 77
Girls						
96	56	60. 41±1. 50	80	62. 17±1. 17	100	65. 34±0. 90
108	59	69. 10±1. 81	103	71. 27±1. 17	100	75. 73±0. 99
120	48	80. 55±1. 88	123	81. 89±1. 05	100	84. 58±0. 92
132	30	89. 30±1. 88	93	91. 76±1. 27	100	93. 48±0. 80
144	28	95. 96±1. 67	95	100. 66±0. 96	100	101. 30±0. 76
156	44	101. 72±1. 28	97	106. 03±0. 63	100	105. 27±0. 64
168	42	107. 62±1. 06	97	109. 71±0. 69	100	108. 34±0. 58

data for each age group. Relatively large numbers of individuals are included in each age group. In general, the results appear satisfactory for reasonably sound conclusions.

The ossification ratios for boys of Amarillo, Lubbock, and Cumberland are uniform throughout, with the exception of those for Lubbock boys aged 13 and 14 years, which indicate a somewhat retarded rate of calcification (table 3, fig. 1). The data for boys in all three cities, however, indicate a bone development less rapid than for the University of Chicago normal children. The data for girls indicate a consistently lower rate of calcification for Lubbock girls than for any other group of girls. The other groups of girls, including the Uni-

Table 4. Mean skeletal age ratings, and their standard errors, of carpal bones of normal children and of children exposed and not exposed to high-fluoride waters

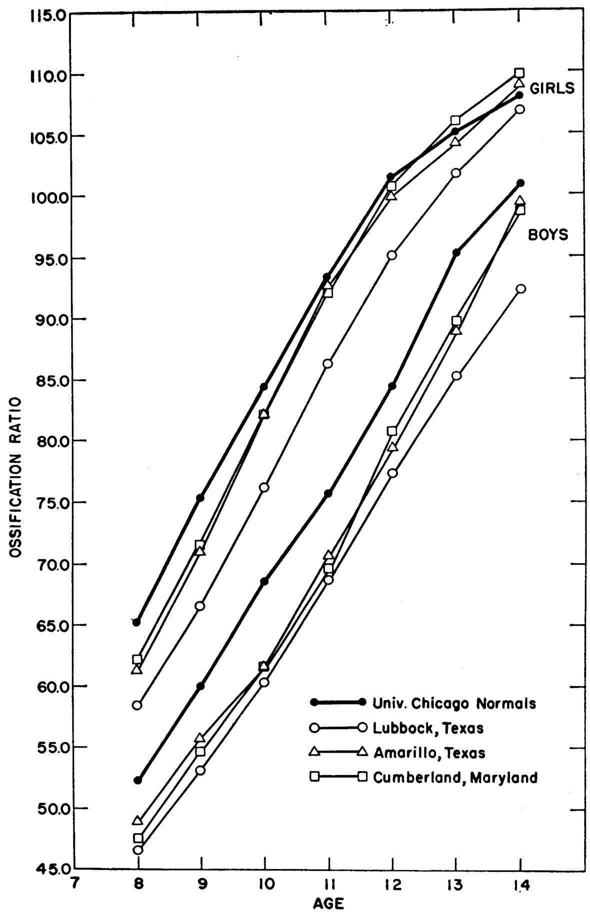
Average chronological age (months)	Fluoride water (3.5–4.5 p.p.m. F) Lubbock, Tex.		Fluoride water (3.3–6.2 p.p.m. F) Amarillo, Tex.		Mottled enamel, moderate or severe, Lubbock and Amarillo, Tex.	
	Number of children	Mean skeletal age rating (months)	Number of children	Mean skeletal age rating (months)	Number of children	Mean skeletal age rating (months)
Boys						
96	69	85. 35±1. 37	42	88. 29±2. 09	53	89. 04±1. 62
108	93	96. 94±1. 11	89	99. 20±1. 75	116	99. 21±1. 46
120	79	111. 00±1. 87	62	109. 94±1. 76	111	110. 30±1. 50
132	79	126. 72±1. 74	66	125. 09±2. 14	110	125. 62±1. 53
144	85	140. 29±1. 48	75	138. 20±1. 51	122	138. 84±1. 20
156	90	150. 73±1. 64	69	151. 00±1. 70	118	150. 61±1. 46
168	70	163. 71±1. 72	38	165. 79±2. 52	87	163. 34±1. 72
Girls						
96	75	89. 00±1. 29	61	90. 05±1. 20	67	90. 04±1. 22
108	90	97. 60±1. 24	120	99. 80±1. 11	130	99. 09±1. 07
120	99	108. 58±1. 36	94	113. 68±1. 51	133	110. 82±1. 22
132	63	124. 43±1. 93	59	129. 81±2. 04	92	126. 72±1. 68
144	78	142. 54±1. 55	57	145. 11±1. 91	90	143. 60±1. 45
156	108	157. 17±1. 39	72	158. 67±1. 41	135	157. 44±1. 14
168	86	170. 23±1. 27	56	175. 07±2. 04	99	171. 57±1. 30

Average chronological age (months)	Mottled enamel, zero or mild, Lubbock and Amarillo, Tex.		Nonfluoride water, no mottled enamel, Cumberland, Md.		University of Chicago normal children	
	Number of children	Mean skeletal age rating (months)	Number of children	Mean skeletal age rating (months)	Number of children	Mean skeletal age rating (months)
Boys						
96	33	81. 91±2. 45	81	87. 22±1. 54	50	96. 7±0. 88
108	54	94. 78±2. 15	96	99. 19±1. 64	50	105. 2±1. 23
120	25	106. 56±3. 11	99	111. 42±1. 71	50	117. 5±1. 13
132	27	126. 33±3. 40	116	123. 76±1. 67	50	128. 4±1. 17
144	33	140. 64±2. 51	99	141. 48±1. 37	50	140. 8±0. 84
156	33	153. 55±1. 88	67	152. 55±1. 96	50	152. 8±0. 94
168	23	167. 35±3. 04	67	164. 46±1. 67	50	167. 4±1. 25
Girls						
96	56	89. 57±1. 39	80	90. 98±1. 12	50	95. 8±1. 26
108	59	98. 28±1. 64	103	101. 85±1. 10	50	108. 2±0. 99
120	48	112. 50±1. 97	123	113. 15±1. 19	50	119. 9±0. 94
132	30	126. 60±2. 75	93	127. 71±1. 79	50	133. 0±1. 07
144	28	144. 85±2. 39	95	144. 60±1. 55	50	145. 8±1. 28
156	44	158. 32±2. 11	97	159. 00±1. 18	50	158. 0±1. 30
168	42	173. 00±2. 27	97	170. 38±1. 42	50	170. 5±1. 00

versity of Chicago normal children, are quite uniform throughout, as shown in figure 1. The data showing ossification ratios of children classified according to the mottled enamel diagnosis indicate uniformity for all ages and for boys and girls in all groups (table 3, fig. 2).

In figure 5, the mean carpal ossification ratios for boys and girls of all ages are compared graphically. The Lubbock boys and girls had the lowest values, and the value for Lubbock boys corresponds to that for boys of both Amarillo and Lubbock who showed little or no mottled enamel. The girls in Lubbock and Amarillo who had moderate or severe mottled enamel compared favorably with both the Cumberland and the University of Chicago girls and with

Figure 1. Mean ossification ratios of carpal bones.



the girls in Lubbock and Amarillo diagnosed as having only mild or no mottled enamel.

Skeletal Age Ratings

For ages 8 through 11 years, the skeletal age ratings for the children in Lubbock, Amarillo, and Cumberland differ from the ratings for the University of Chicago children (table 4, fig. 3). However, at ages 12, 13, and 14 years, all groups agreed remarkably well. When the children were classified according to mottled enamel diagnosis, all groups demonstrated uniformity in skeletal age ratings (table 4, fig. 4).

As shown in figure 5, the data for mean skeletal age ratings suggest some advanced development for Lubbock girls and perhaps for both boys and girls of Amarillo and Lubbock who had moderate or severe mottled enamel. This finding was not apparent, however, when the Amarillo boys and girls were considered as a group regardless of the mottled enamel diagnosis.

Sex Differences

The repeated observations of advanced skeletal maturity in girls, as compared with boys, from birth through the growing years is confirmed in the findings in this study. Sex differences in skeletal development are particularly evident in comparisons of the ossification ratios (tables 3 and 4, figs. 1, 2, and 5). They are suppressed in comparisons of skeletal age ratings because of the use of separate standards for boys and girls (figs. 3, 4, and 5). Between ages 7 and 12 years, average osseous development in the girls apparently proceeded approximately at the same rate as in boys, as shown by the slope of the curves, but was advanced about 2 years over that of the boys. This lead was reduced in the next 2 years as the girls

Figure 2. Mean ossification ratios of carpal bones.

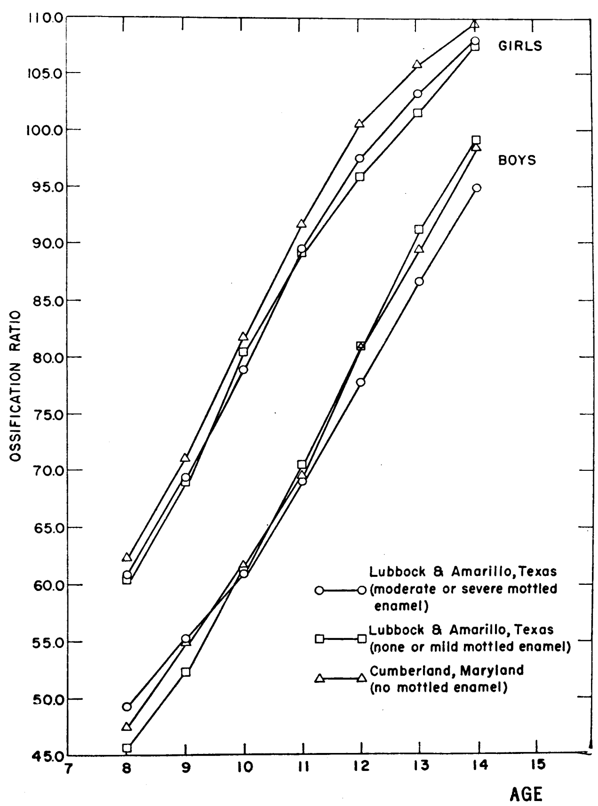
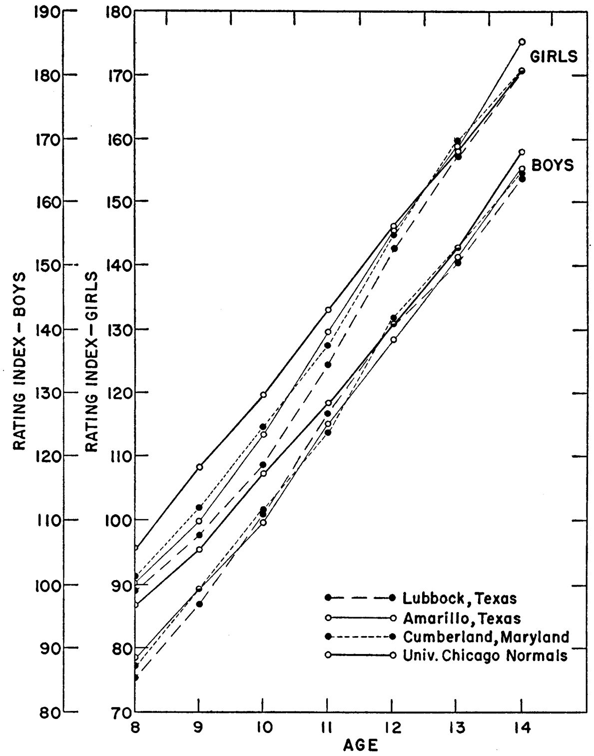


Figure 3. Skeletal age rating index as determined by carpal bone calcification.



approached maturity and the boys continued to grow at the same rate as before.

Discussion

Continuous exposure to relatively high levels of waterborne fluoride apparently failed to influence the calcification of the carpal bones of children aged 7 through 14 years. This result appears evident in the high order of agreement in the data obtained on three location groups of children, with and without exposure to waterborne fluoride.

Minor differences occurred in the weighted mean carpal ossification ratios and in the mean skeletal age ratings for the University of Chicago, Amarillo, Lubbock, and Cumberland children, but these differences appear not to be associated with the exposure to high-fluoride water received by the Amarillo and Lubbock children. The data suggest some tendency toward a uniformly lower osseous development among Lubbock children, particularly girls, but not among Amarillo girls or boys. However, since children in both communities were exposed to fluoride waters, this suggested difference may be related to other factors.

It has been reported that the progress of ossification may be influenced by environmental conditions (*29*, *30*), extremes in climate (*31*), systemic disorders (*30*, *32*), and endocrine functions (*32*). Lubbock and Amarillo are within 150 miles of each other, but they differ somewhat in environmental surroundings. Lubbock is a relatively new community, the seat of a large technologic college, and the center of an agricultural area. Amarillo is a much older town and is surrounded by cattle ranges. The populations in the two communities may therefore differ somewhat in their hereditary and ethnic background and in general day-to-day activities. The effects of environmental variables on bone development among the children of these towns, however, are purely speculative.

As previously mentioned, the most pronounced nondental effect of excessive quantities of fluorine is an advanced calcification in both skeletal and ligamentous tissues (*1–4*). Experimental studies with animals have also given

Figure 4. Skeletal age rating index as determined by carpal bone calcification.

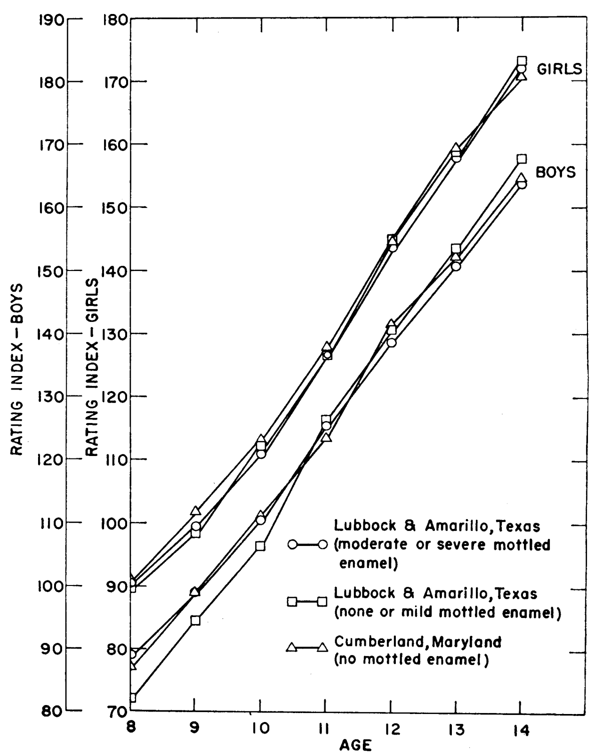
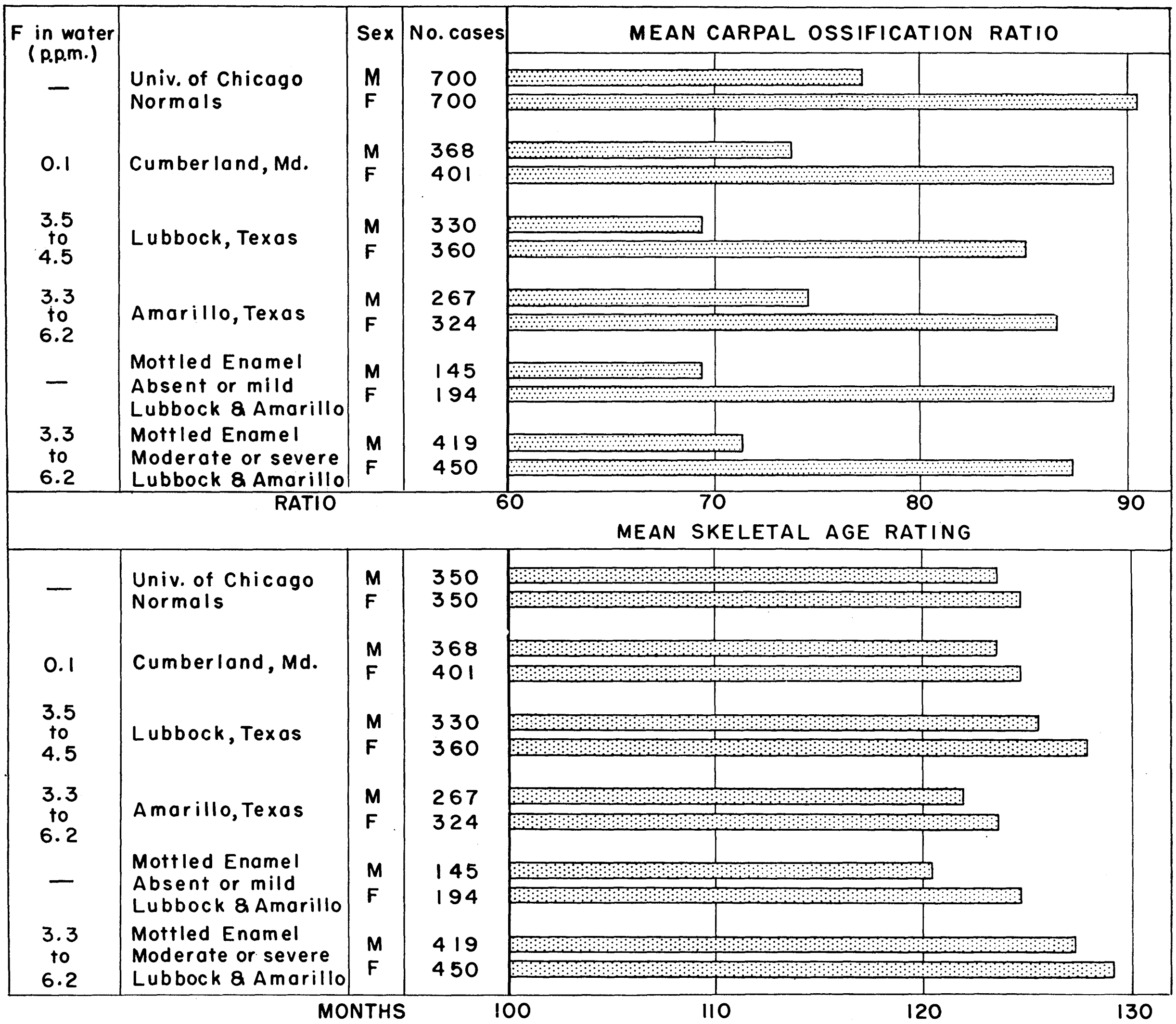


Figure 5. Mean carpal ossification ratios and skeletal age ratings for groups of children with and without exposure to high-fluoride waters.



evidence that a high-fluorine intake is identified with skeletal hypercalcification (*33–36*). Results in these latter studies are based generally on analytical data. Inconsistencies in the data are attributed mainly to variations in calcium intake as well as to the extent and duration of the fluoride exposure. In general, relatively excessive quantities of fluoride must be ingested by experimental animals to produce calcification changes, as shown by ash, calcium, or phosphorus analyses. For example, in a recent report (*36*), as much as 50 p.p.m. F in the drinking water of growing experimental rats caused a more than fivefold increase in the fluorine content of mandibles and femurs without affecting the amount of ash, calcium, or phosphorus or the calcium : phosphorus ratio of the ash. More recent attempts to assess the relation of fluorine to calcium metabolism of skeletal tissues have made use of Ca^{45} (*37*, *38*). These studies have failed to produce evidence of any pronounced effect of relatively high levels of fluorine on the calcium metabolism of skeletal tissues.

A survey of the previous experiences with fluorine, both clinically and experimentally, in respect to skeletal tissue development, therefore, gives every reason to expect that if any effects were to be found in the present study of the development of the carpal bone in children, they would be in the nature of hypercalcification and advanced skeletal maturity and bone development. The calcification data accumulated in this study do not indicate the occurrence of this characteristic skeletal effect of fluorine among the children drinking the fluoride waters of Lubbock and Amarillo. Apparently, approximate levels of 3.5 to 5.0 p.p.m. F in the drinking water are not sufficient to affect calcification in skeletal tissues which are developing at ages 7 through 14 years. The presence of 3.5 to 5.0 p.p.m. F in the drinking water also has not altered the long-established sex differences in the rate of development.

Previously in this report, evidence was cited which showed that the development of bones of the hand and wrist parallels that of the rest of the skeleton. On the basis of this evidence, it seems justified to suggest that skeletal development throughout the body was not affected by the exposure to high-fluoride water received by the Lubbock and Amarillo children. There may be some consistency in this finding and previous evidence that age, height, and weight relations and bone-fracture experience are not influenced by exposure to high-fluoride waters (*10*). A number of the persons included in the previous study lived in Amarillo and Lubbock or their immediate environs.

The results of this study apply to the continuous exposure to drinking water containing approximately 3.5 to 6.2 p.p.m. F, quantities considerably larger than the approximately 1.00 p.p.m. F added to drinking water for the partial control of dental caries. There is every justification for concluding from these results, therefore, that this added 1.00 p.p.m. will not be detrimental to the skeletal development of children as shown by the progress of calcification in the carpal bones.

Summary

Exposure to fluoride in drinking water was studied for evidence of detrimental effects on skeletal calcification and bone development in children. Three groups of children aged 7 through 14 years, living in Lubbock and Amarillo, Tex., and Cumberland, Md., were selected on the basis of continuous exposure to their communal drinking waters, which contained fluoride in the amounts of 3.5 to 4.5 p.p.m. F, 3.3 to 6.2 p.p.m. F, and 0.1 p.p.m. F, respectively. Radiographs were taken of the right hand and wrist of 2,050 children. From these X-rays, the skeletal age was assessed and a quantitative index of ossification was determined.

No evidence, available by radiographs, was obtained which would indicate that there was any adverse effect on the carpal bones or on their growth and development as a consequence of the continuous use of drinking water containing approximately 3.5 to 6.2 p.p.m. F. These results confirm the safety of maintaining the fluoride level of public water supplies at about 1.00 p.p.m. F, by controlled fluoridation, for the reduction of tooth decay.

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REFERENCES

(*1*) Roholm, K.: Fluorine intoxication. A clinical hygienic study. London, H. K. Lewis, 1937.

(*2*) Moller, P. F., and Gudjonsson, S. V.: Massive fluorosis of bones and ligaments. Acta Radiol. 13: 269–294 (1932).

(*3*) Shortt, H. E., McRobert, G. R., Barnard, T. W., and Nayer, A. S. M.: Endemic fluorosis in the Madras Presidency. Indian J. M. Research 25: 553–568 (1937).

(*4*) Pandit, C. G., Raghauachari, T. N. S., Rao, D. S., and Kirshuamurti, N.: Endemic fluorosis in south India. A study of the factors involved in the production of mottled enamel in children and severe bone manifestations in adults. Indian J. M. Research 28: 533–558 (1940).

(*5*) Ockerse, T.: Endemic fluorosis in the Pretoria district. South African M. J. 15: 261–266 (1941).

(*6*) McClure, F. J.: Non-dental physiological effects of trace quantities of fluorine. *In* Dental caries and fluorine. Edited by F. R. Moulton. Washington, D. C., American Association for the Advancement of Science, 1946.

(*7*) Dean, H. T.: The investigation of physiological effects by the epidemiological method. *In*

Fluorine and dental health. Edited by F. R. Moulton. Washington, D. C., American Association for the Advancement of Science, 1946.

(8) McClure, F. J., and Kinser, C. A.: Fluoride domestic waters and systemic effects. II. Fluorine content of urine in relation to fluorine in drinking water. Pub. Health Rep. 59: 1575–1591 (1944).

(9) McClure, F. J., Mitchell, H. H., Hamilton, T. S., and Kinser, C. A.: Balances of fluorine ingested from various sources in food and water by five young men. Excretion of fluorine through the skin. J. Indust. Hyg. and Toxicol. 27: 159–170 (1945).

(10) McClure, F. J.: Fluoride domestic waters and systemic effects. I. Relation to bone fracture experience, height, and weight of high school boys and young selectees of the armed forces of the United States. Pub. Health Rep. 59: 1543–1558 (1944).

(11) Hodges, P. C., Fareed, O. J., Ruggy, G., and Chudnoff, J. S.: Skeletal sclerosis in chronic sodium fluoride poisoning. J. A. M. A. 117: 1938 (1941).

(12) Lantz, E. M., Smith, M. C., and Leverton, R. M.: The calcium and phosphorus metabolism of children with mottled enamel. J. Home Econ. 27: 1–4 (1935).

(13) Glock, G. E., Lowater, F., and Murray, M. M.: The retention and elimination of fluorine in bones. Biochem. J. 35: 1235–1239 (1941).

(14) Chemicals in foods and cosmetics. *In* Hearings before the House Select Committee to Investigate the Use of Chemicals in Foods and Cosmetics. House of Representatives, 82d Cong. 2d sess. Washington, D. C., U. S. Government Printing Office, 1952.

(15) Ranke, J.: [Über die ossificationsvorgänze. A discussion.] Münch. med. Wchnschr. 43: 686 (1896).

(16) Pryor, J. W.: Development of the bones of the hand as shown by the X-ray method. Bull. State Coll. Kentucky, series 2, No. 5, June 1905.

(17) Pryor, J. W.: Some observations of the ossification of the bones of the hand. Bull. Univ. Kentucky, series 8, No. 11, 1916.

(18) Pryor, J. W.: Time of ossification of the bones of the hand of the male and female and union of epiphyses with the diaphyses. Am. J. Phys. Anthropol. 8: 401–410 (Oct.–Dec. 1925).

(19) Flory, C. D.: Osseous development of the hand as an index of skeletal development. Monograph Soc. Res. Child Develop., vol. 1, No. 3. Washington, D. C., National Research Council, 1936.

(20) Todd, T. W.: Atlas of skeletal maturation (hand). St. Louis, C. V. Mosby Co., 1937.

(21) Greulich, W. W., and Pyle, S. I.: Radiographic atlas of skeletal development of the hand and wrist, based on the Brush Foundation study of human growth and development initiated by T. Wingate Todd. Stanford University, Calif., Stanford University Press, 1950.

(22) Baldwin, B. T.: The physical growth of children from birth to maturity. Univ. of Iowa Studies in Child Welfare 1: No. 1 (1st series, No. 50). Iowa City, The University, 1921.

(23) Baldwin, B. T., Busby, L. M., and Garside, H. V.: Anatomic growth of children: A study of some bones of the hand, wrist, and lower forearm by means of roentgenograms. Univ. of Iowa Studies in Child Welfare 4; No. 1 (1st series, No. 164). Iowa City, The University, 1928.

(24) Carter, T. M.: Technique and devices used in radiographic study of the wrist bones of children. J. Educ. Psychol. 17: 237–247 (1926).

(25) Kelly, H. J.: Anatomic age and its relation to stature. Univ. of Iowa Studies in Child Welfare 12: No. 5 (new series, No. 331). Iowa City, The University, 1937.

(26) MacNair, V., and Roberts, L. J.: Effect of a milk supplement on the physical status of institutional children. II. Ossification of the bones of the wrist. Am. J. Dis. Child. 56: 494–509 (1938).

(27) MacNair, V.: Effect of a dietary supplement on ossification of the bones of the wrist in institutional children. II. Effect of a cod liver oil supplement. Am. J. Dis. Child. 58: 295–319 (1939).

(28) Dean, H. T., and Elvove, E.: Some epidemiological aspects of chronic endemic dental fluorosis. Am. J. Pub. Health 26: 567 (1936).

(29) Todd, T. W.: Roentgenographic appraisement of developmental growth in the skeleton. *In* Growth and development of the child. IV. Appraisement of the child. White House Conference on Child Health and Protection. New York, Century Co., 1932, pp. 258–285.

(30) Francis, C. C.: Factors influencing the appearance of centers of ossification during early childhood. Am. J. Dis. Child. 57: 817–830 (1939).

(31) Galstaun, G.: Some notes on the union of epiphyses in Indian girls. Indian Med. Gaz. 65: 191–192 (1930).

(32) Engelbach, W., and McMahon, A.: Osseous development in endocrine disorders. Endocrinology 8: 1–53 (1924).

(33) Greenwood, D. A., Hewit, E. A., and Nelson, V. E.: Effects of fluorine on respiration, blood pressure, coagulation, and blood calcium and phosphorus in the dog. J. Am. Vet. M. A. 86 (new series, 39): 28–42 (1933).

(34) Du Toit, P. J., Smuts, D. B., and Malan, A. J.: Fluorine metabolism in rats and bovines. Oderstepoort J. Vet. Sc. and Animal Indust. 8: 359–374 (1937).

(35) McClure, F. J., and Mitchell, H. H.: The effect of fluorine on the calcium metabolism of albino

rats and the composition of bones. J. Biol. Chem. 90: 297–320 (1931).

(36) McClure, F. J.: Availability of fluorine in sodium fluoride vs. sodium fluosilicate. Pub. Health Rep. 65: 1175–1186 (1950).

(37) Gordonoff, T., and Minder, W.: Versuche mit Ca^{45} zum Caries-Fluor-Problem. Helvet. Physiol. Pharmacol. Acta 9: C24, C25 (Feb. 1951).

(38) Comar, C. L., Visek, W. J., Lotz, W. E., and Rust, J. H.: Effects of fluorine on calcium metabolism and bone growth in pigs. Am. J. Anat. 92: 361–375 (1953).

(39) Likins, R. C., Zipkin, I., McClure, F. J., and Steere, A.: Effect of fluorine on the metabolism of calcium and phosphorus in the rachitic rat. J. Dent. Research 32: 665 (1953).