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X-ray Changes in the Forearm and Crus of Residents of Areas in Jilin Province with Varying Drinking Water Fluoride Concentrations

HUANG Changqiang
Department of Endemic Fluorosis, Jilin Province No. 1 Institute for Prevention and Treatment of Endemic Diseases, Baicheng 137000; Email：huangcq888@163.com

[Abstract] Goal To understand the characteristics of forearm and crus X-rays of residents from areas with varying concentrations of fluoride in their drinking water, providing evidence for diagnosis of osteofluorosis. **Method** Using quantificational epidemiological methods, a total of 15 villages from Qianan and Nonan Counties of Jilin Province were selected as the subjects of the investigations; these villages all had at least 50 years of history, complete records of drinking water fluoride levels for that period with stable levels, no industrial or coal-burning fluoride pollution, no other sources of fluoride, and no low-fluoride drinking water alternatives. Fluoride concentration was determined and the areas were divided into 11 fluoride concentration levels (from 0.5 to 7.0 mg/L), and then from each range subjects ages 16-60 that had lived in the area for at least 10 years were selected. We considered 5 age ranges with cutoffs at 21, 31, 41, and 51, and a random selection of 10 to 15 subjects was made from each age range and the forearm and crus of was examined by x-ray. The 0.5-1.0 mg/L group were regarded as the low fluoride (control) group, and the 1.5-7.0 mg/L range was considered the high fluoride group; the two groups were compared with respect to various x-ray signs and disease detection rates. **Result** The x-ray examination showed three kinds of changes: osteofluorosis, articular degeneration, and osteoporosis. Of these, articular degeneration was the most common, with the detection rates of the high fluoride group (31.55%, 153/485) higher than the low fluoride group (21.58%, 41/190), a statistically significant difference (χ^2=6.62,p< 0.01). Among the 675 subjects, 72 were diagnosed with osteofluorosis, with most of them occurring in the high fluoride group (χ^2=25.65,p< 0.01).When the fluoride concentration reaches 6.0-7.0 mg/L, the detection rate increases markedly, to 44.92% (53/118). Regardless of fluoride concentration or degree of osteofluorosis, the most prevalent x-ray sign was change to the periosteum, reaching 95.83% (69/72), articular changes were second with 79.17%, 57/72), and changes to trabecular patterns were observed least (56.94%,41/72); the differences between the three were statistically significant (χ^2=9.64, p<0.01). Regardless of fluoride concentration, there was degeneration of the elbow, knee, and wrist joints, the detection rate was highest for the elbow joint (17.78%, 120/675), followed by the knee (15.41%, 104/675), and wrist degeneration was observed the least (7.53%, 53/675), the differences between the three were statistically significant (χ^2=30.74, p<0.01). The detection rate for articular degeneration of the elbow for the high fluoride group (21.03%, 102/485) was markedly higher than the low fluoride group (9.47%, 18/190, χ^2=12.47, p<0.01). Of the 35 signs detectable by x-ray examination, most were found in both high and low fluoride groups; periosteal changes were rarely seen in the low fluoride group, and often seen in the high fluoride group. **Conclusion** The signs of osteofluorosis in detectable in x-rays are quite varied and complex, when x-rays are used for diagnosis a comprehensive analysis should be carried out based on all the various signs and an overall determination made; only then will a diagnosis be correct and reliable.

[Key Words] Endemic disease; fluoride poisoning; osteofluorosis; bones and joints; x-ray

X-ray examinations are an important way of detecting osteofluorosis and have been a common diagnostic tool for many years.[1] However, this method not only requires specialized equipment, but also is limited by local conditions and technological ability. In order to simplify its use, our current national “Diagnostic Criteria for Endemic Osteofluorosis”

recommends the use of the forearm and crus, which are relatively easy to x-ray for the purposes of diagnosing osteofluorosis.[2] The endemic fluoride poisoning monitoring item of the current central fund for improving local health and hygiene also requires x-ray examinations of the forearm and crus.[3] In order to further understand the common x-ray signs seen in the forearm and crus with the goal of providing more reliable diagnosis of osteofluorosis, the author has carried out an investigation of the x-ray signs in the forearm and crus of residents of areas with varying concentrations of fluoride in their drinking water, the results are as follows.

1. Subjects and method

1.1. Location: From Qianan and Nonan Counties of Jilin Province, a total of 15 villages were selected as the location of the investigation. These villages all had at least 50 years of history; complete records of drinking water fluoride levels for that period with a variation of no more than 0.3 mg/L in well fluoride concentration; residents with no habit of drinking tea; low population mobility; no major difference with respect to ethnicity, the natural environment, level of economic development, means of work, lifestyle, etc.; no industrial or coal-burning fluoride pollution; no other sources of fluoride; and no low-fluoride drinking water alternatives.

1.2. Fluoride concentration testing and division into groups: From the 15 villages, water samples were taken and fluoride concentration determined using the ion selective electrode method. The villages were divided into 11 groups based on their fluoride concentration, with groups at 0.5, 1.0, 1.5, 2.0, 2.2, 2.4, 3.0, 3.5, 4.0, 6.0, and 7.0 mg/L. For convenient comparison, the 0.5-1.0 mg/L group was regarded as the low fluoride (control) group, and the 1.5-7.0 range was considered the high fluoride group.

1.3. Subjects: From the residents of villages at each concentration level subjects between the age of 16 and 60 and who had lived in the village for at least 10 years were selected. The subjects were divided into 5 age groups with cutoffs at 21, 31, 41, and 51; there were 10-15 subjects from each age group from each fluoride level, with an even balance of male and female, a total of 675 subjects were selected in all.

1.4. Examination methods: Frontal x-rays were taken of the forearm (including the elbow) and the crus (including the knee). Baseline x-ray presentations, osteofluorosis x-ray presentations, detection rates for various x-ray signs for osteofluorosis, detection rates for major x-ray signs distinguishing the degree of osteofluorosis, detection rate for articular degeneration of the elbow, knee, and wrist for various fluoride levels were calculated.

1.5. Diagnosis standard: diagnosis of osteofluorosis was made according to "Endemic Osteofluorosis Diagnostic Standards" (WS 192-2008)[2]

1.6. Statistical analysis: SPSS 11.5 software was used for statistical analysis. The comparison of differences in the detection rates used a $\chi 2$ test; $p < 0.05$ indicates a statistically significant difference.

2. Results

2.1. Fluoride testing: The drinking water fluoride levels of the villages are: Xiaowangjia Village, Rangzijing Village, 0.5 mg/L; Xigengjia Village, Zhongrenzi Village, 1.0 mg/L; Majiawo Village, Jianzijing Village, 1.5 mg/L; Linjia Village, 2.0 mg/L; Xiguang Village, 2.2 mg/L; Bijiadian Village, 2.4 mg/L; Dongcang Village,

Huangtai Village, 3.0 mg/L; Houxun Village, 3.5 mg/L; Jiangjia Village, 4.0 mg/L; Yexiaopu Village, 6.0 mg/L; Anzijing Village, 7.0 mg/L.

2.2. Major x-ray changes in the forearm and crus between high and low fluoride groups: Table 3 has three major changes visible in x-rays; of them, articular degeneration is the most common change, with a fairly high detection rate. The detection rate of the high fluoride group is higher than the low fluoride group, and the difference is statistically significant (χ^2=6.62, p< 0.01). A total of 72 subjects were diagnosed with osteofluorosis, with the majority coming from the high fluoride group (χ^2=25.65, p< 0.01). In the low fluoride group we saw two women with changes consistent with osteofluorosis; under investigation, it was found that they had lived in a high fluoride area before marriage. The results of our investigation indicate that fluoride intake has no direct relationship to the incidence of osteoporosis.

Table 1: Major x-ray changes in forearm and crus between high and low fluoride groups

Group	*n*	Articular Degeneration		Osteofluorosis		Osteoporosis	
		n	Detection rate (%)	*n*	Detection rate (%)	*n*	Detection rate (%)
High fluoride	485	153	33.55*	70	14.34b	30	6.19
Low fluoride	190	41	21.58	2	1.05	13	6.84
Total	675	194	28.74	72	10.67	43	6.37

Note: compared to low fluoride group, *$p<0.05$, b$p<0.01$

2.3. Detection rate and major x-ray signs for subjects with varying drinking water fluoride concentrations: Table 2 indicates that when fluoride concentration is at or above 1.0 mg/L, the average detection rate for osteofluorosis is 12.52%. In the 1.0-2.0 mg/L range or the 2.2-4.0 mg/L range, the detection rate is not high, 2.33% and 5.79%, respectively. For subjects with drinking water in the 6.0-7.0 mg/L range, the detection rate was markedly higher, reaching 44.92% (53/118). The difference in detection rate between fluoride concentrations in the 1.0-2.0 mg/L and 6.0-7.0 mg/L range was statistically significant (χ^2=172.16, p< 0.05). Among the three kinds of changes, periosteal, articular, and trabecular pattern changes, periosteal changes were most common, followed by articular changes; changes to the trabecular pattern were relatively rare. The differences in detection rate between the three are statistically significant (χ^2=9.64, p< 0.01). However, across the three types there is no clear relationship between the increased rates of detection of these changes and increased fluoride concentration (χ^2=1.58, 0.71, 0.19, average p> 0.05).

Table 2: Detection rate and major x-ray signs for subjects with varying drinking water fluoride concentrations

Fluoride Concentration (mg/L)	*n*	Osteofluorosis		Periosteal Changes		Articular Changes		Trabecular Pattern Changes	
		n	Detection rate (%)	*n*	Detection rate (%)	*n*	Detection rate (%)	*n*	Detection rate (%)
6.0-7.0	118	53	44.92	51	97.23	41	77.36	36	67.92
2.2-4.0	242	14	5.79	13	92.87	12	85.71	7	50.00
1.0-2.0	215	5	2.33	5	100.00	4	80.00	2	40.00
Total	575	72	12.52	69	28.74	57	79.19	45	59.21

2.4. Major x-ray signs and detection rate for osteofluorosis sufferers at varying degrees of severity: As Table 3 shows, osteofluorosis sufferers often see periosteal changes, and this is consistent across all severities of the disease, see Figure 1. Even light sufferers saw a detection rate for periosteal changes of 100%. Trabecular pattern changes were rarely seen in light cases, but there was marked increases in moderate and severe sufferers. Articular changes had a high prevalence in light cases (88.00%), and was often seen relatively often in the medium to severe cases. However, there was no statistically significant relationship between severity and detection rates for either trabecular pattern changes or articular changes (χ^2=1.64, 1.27, p> 0.05).

Table 3: Major x-ray signs and detection rate for osteofluorosis sufferers at varying degrees of severity

X-ray severity classification	Cases of Osteofluorosis	Periosteal Changes		Articular Changes		Trabecular Pattern Changes	
		n	Detection rate (%)	*n*	Detection rate (%)	*n*	Detection rate (%)
Early	31	28	90.32	20	64.52	11	35.48
Light	25	25	100.00	22	88.00	15	60.00
Moderate	15	15	100.00	11	93.33	11	93.33
Severe	1	1	100.00	1	100.00	1	100.00
Total	72	69	95.83	54	75.00	38	52.77

2.5. Detection rate for articular degeneration of the elbow, knee, and wrist for subjects with varying drinking water fluoride concentrations: From Table 4 we can see that all groups showed some articular degeneration of the elbow, knee, and wrist; overall, degeneration of the elbow was most common, followed by the knee and then the wrist. The difference between the three was statistically significant (χ^2=30.74, 1.27, p< 0.05). For all the joints, there is no clear relationship between increase in degeneration and increase in fluoride

concentration: the detection rates for 0.5, 1.0, 1.5, 2.0-2.4, 3.0-4.0 mg/L are fairly close, with no consistency to the differences, only at 6.0-7.0 mg/L range is there a major increase in the detection rate for all joints, the difference between the three types of degeneration is statistically significant (χ^2=124.36, p< 0.01).

Table 4: Detection rate for articular degeneration of the elbow, knee, and wrist for subjects with varying drinking water fluoride concentrations:

Fluoride Concentration (mg/L)	*n*	Elbow Degeneration		Knee Degeneration		Wrist Degeneration	
		n	Detection rate (%)	*n*	Detection rate (%)	*n*	Detection rate (%)
6.0-7.0	118	42	53.59	35	29.66	11	16.10
3.0-4.0	146	22	15.07	24	16.44	15	5.48
2.0-2.4	138	18	13.04	9	6.52	11	3.62
1.5	83	20	24.10	13	15.66	1	7.23
1.0	90	14	15.56	12	13.33	8	8.89
0.5	100	4	4.00	11	11.00	7	7.00
Total	675	120	17.78	104	79.17	53	7.85

2.6. Comparison of the detection rate for articular degeneration of the elbow, knee, and wrist for high and low fluoride groups: The detection rate for elbow degeneration of the high fluoride group is 21.04% (102/485), for the low fluoride group it is 9.47% (18/190, χ^2=124.36, p< 0.01). The detection rate for wrist degeneration of the high fluoride group is 7.84% (38/485), for the low fluoride group it is 7.89% (15/190, χ^2=0.001, p> 0.05). The detection rate for knee degeneration of the high fluoride group is 16.70% (81/485), for the low fluoride group it is 12.11% (23/190, χ^2=2.21, p> 0.05).

2.7. Major x-ray signs in the forearm and crus for the high and low fluoride groups: we examined 35 x-ray signs in the forearm and crus for the high and low fluoride groups; among those, 19 signs had a fairly high incidence rate: see Table 5. The major x-ray signs can be grouped into periosteal changes, trabecular pattern changes, and articular changes, see Figure 1. Among these changes, most occurred in the high fluoride group and also in the low fluoride group. Among the changes which occurred, the detection rate of periosteal changes was lower than the articular and trabecular pattern changes in the low fluoride group. Some of these changes occurred only in the high fluoride group, indicating that periosteal changes are more distinctive than articular and trabecular pattern changes; x-ray changes that appear in both high and low fluoride groups are not osteofluorosis-specific signs.

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Table 5: Major x-ray signs in the forearm and crus for the high and low fluoride groups

[*n*, detection rate (%)]

Group	*n*	Trabecular Pattern, Bone Density Changes			
		Osteosclerosis	Osteoporosis	Abnormal trabecular pattern in wrist	Abnormal trabecular pattern in knee
High Fluoride	485	10(2.1)	30(6.2)	49(10.1)	28(5.8)
Low Fluoride	190	0(0.0)	8(4.2)	10(5.3)	7(3.7)
Group	*n*	Forearm periosteal changes			
		Abnormal interosseous crest of radius[a]	Changes to the interosseous membrane[b]	Changes at attachment site of the pronator teres[c]	
High Fluoride	485	36(7.4)	36(7.4)	70(14.4)	
Low Fluoride	190	2(1.1)	0(0.0)	14(7.4)	
Group	*n*	Crus periosteal changes			
		Periosteal proliferation	Calcification of the interosseous membrane	Thickening of tibia at attachment site of fibular collateral ligament	Osteophyma of the fibular capitulum
High Fluoride	485	12(2.5)	19(3.9)	17(3.5)	11(2.3)
Low Fluoride	190	0(0.0)	0(0.0)	0(0.)	0(0.0)
Group	*n*	Elbow joint changes			
		Coronoid process hyperplasia	Cystic changes under the articular surface of the radial head	Hypertrophy of the radial head	
High Fluoride	485	66(13.6)	54(11.1)	22(4.5)	
Low Fluoride	190	9(4.7)	9(4.7)	5(2.6)	
Group	*n*	Knee joint changes			
		Hyperplasia of the intercondylar eminence		Hypertrophy of the articular margin	
High Fluoride	485	62(12.8)		20(4.1)	
Low Fluoride	190	20(10.5)		3(1.6)	
Group	*n*	Wrist joint changes			
		Cystic changes of the lunate	Cystic changes of the triquetral	Cystic changes of the scaphoid	
High Fluoride	485	30(6.2)	20(4.1)	12(2.5)	
Low Fluoride	190	10(5.3)	8(4.2)	6(3.2)	

Notes (for Table 5): a: Abnormal interosseous crest of the radius includes widening of the interosseous crest, free margin sclerosis, and coarsening of the surface. b: Changes to the interosseous membrane include: formation of sprouting protrusions, wave-shaped, thorn-shaped, triangular, chunky, or other irregular shapes. c: Changes at attachment site of the pronator teres include: Only layering; layering and thickening; layering, thickening, and coarsening of the surface; coarsening with peaks and valleys.

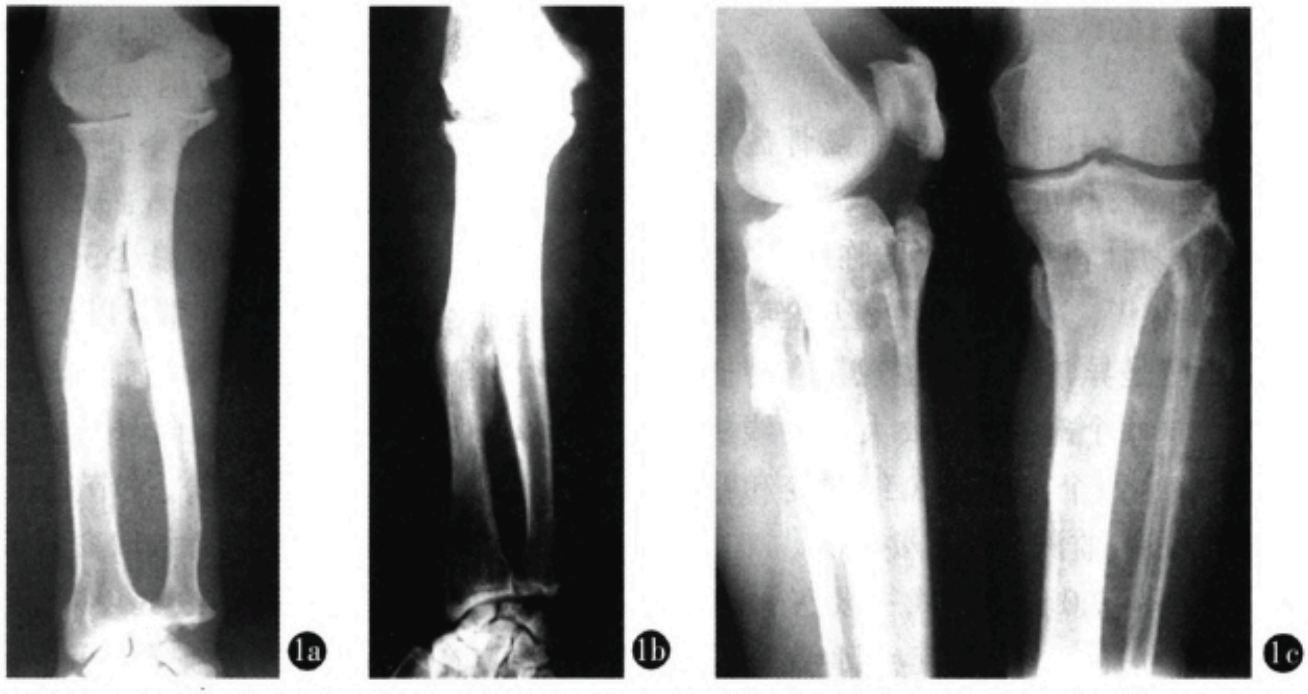

Figure 1: 1a, 1b Frontal x-rays of the forearms of osteofluorosis patients: shows an increase in bone density, a coarsening and disordering of the trabecular pattern of capitulum of the humerous and the proximal and distal radius, fusing of the trabeculae, thickening of the periosteum, narrowing of the medullary cavity, osteosclerosis; the interosseous membrane shows ossification into fin-shaped chucks, and there is thickening and layering at the attachment site of the pronator teres; at the joint, there is coronoid process hyperplasia, narrowing of the joint space, and cystic changes under the articular surface of the radial head. 1c Frontal x-ray of the crus of an osteofluorosis patient: shows thickening and disorder of the trabecular pattern, an increase in bone density, large osteophytes or extensive ossification of the soft tissue; ossification of the interosseous membrane, the patellar attachment site of the quadriceps femoris, the attachment site of the patellar ligament on the tibial tuberosity, and the soleal line; clear hyperplasia of the intercondylar eminence.

3. Discussion

Endemic fluoride poisoning is a disease which effects the entire body,[4] and osteofluorosis is a major phase of this disease, and one of its key manifestations.[5] The most important characteristics of osteofluorosis are the clinical symptoms of damage to the bones and joints as well as a series of x-ray signs.[1] These signs may be present in bones throughout the body, but the forearm and crus are two parts of the body where abnormalities often appear and where the changes are very characteristic of the disease. Taking X-rays of these two body parts

does not require large x-ray machines, and so better understanding the characteristics of x-ray changes in these areas is very important for the diagnosis, prevention, treatment, and monitoring of fluoride poisoning.

When the fluoride concentration of drinking water is in the 0.5-7.0 range, the major changes, based on differences in the detection rate, are articular degeneration, osteofluorosis, and osteoporosis. Although articular degeneration is very common in both high and low fluoride groups, the detection rate in the high fluoride group (31.55%) is clearly higher than the low fluoride group (21.58%), indicating that the articular degeneration present is not limited to the natural changes that would normally be seen in the population, but rather that the excess intake of fluoride is increasing the opportunity for damage.[6-7] The detection rate of osteofluorosis is markedly higher in the high fluoride group precisely because excessive fluoride causes osteofluorosis. Among subjects with drinking water fluoride concentrations of 0.5-1.0 mg/L, we saw two instances of osteofluorosis, presenting as periosteal changes to the forearm; these two cases were both women who had moved from high fluoride areas, and therefore their x-ray changes did not reflect the low fluoride concentration of their current drinking water source. This situation is a reminder that, due to migration, osteofluorosis might occur even in low fluoride areas. The rate of osteoporosis in the high and low fluoride groups was similar, with no statistically significant difference between the two. Osteofluorosis sufferers sometimes show osteoporosis, which can happen in bones throughout the body, but is more often limited to a single bone, or even just certain parts of a single bone.[5] From this perspective, osteofluorosis-induced osteoporosis is different than more common types of osteoporosis, which typically affect the entire body.[8]

At relatively low concentrations of fluoride, detection rates of osteofluorosis are also low: for example, at 1.0-2.0 mg/L and 2.3-4.0 mg/L, the detection rates are only 2.33% and 5.79%, respectively. When the fluoride concentration reaches 6.0-7.0 mg/L, the osteofluorosis detection rate markedly increases to 44.92%. This result suggests that, in the process of fluoride poisoning, although there are many aspects to the damage, in general the higher intake of fluoride results in more bone damage: this is the key cause of osteofluorosis.

When diagnosing osteofluorosis, the major x-ray signs include 3 aspects: changes to the [trabecular] bone, the periosteum, and the joints. This is consistent in results taken from x-ray examinations of bones from all over the body (e.g. the pelvis, the lumbar vertebrae, the forearm, and the crus).[9] Among these three changes, periosteal changes are more commonly detected, followed by articular changes, and then [trabecular] bone changes. The severity of the osteofluorosis will influence the detection rate of each kind of x-ray changes; in particular, periosteal changes are apparent even in the early stages of osteofluorosis, and are found throughout the progression of the disease, in light, moderate and severe cases. [Trabecular] bone and articular changes are not often found in light cases of osteofluorosis, but are more often visible in relatively severe cases. The results above indicate that the periosteal changes of the forearm and crus can be used as primary indicators to diagnose osteofluorosis.

For various levels of fluoride concentration, the detection rate of x-ray signs of articular degeneration is ordered from highest to lowest as follows: elbow joint > knee joint > wrist joint, indicating that the elbow is at the greatest risk in high fluoride environments. X-ray signs due to osteofluorosis appear throughout the body, in the forearm

and crus alone there are 35 different signs; however, it is not the case that all of the signs are sufficient indicators for diagnosis of osteofluorosis. Some of these signs appear only in the high fluoride groups, while some appear even in the subjects with 1.0 mg/L or less, for instance light trabecular pattern changes, osteoporosis, hyperplasia of the joint margin, and other articular degeneration. Trabecular pattern changes alone may be influenced by physical stress or other factors. For instance, trabecular pattern and cystic changes in the wrist might be the result of wrist strain from agricultural labor. There are over 20 possible causes for osteoporosis,[10] and hyperplasia of the joint margin is a change which is common in the normal population.[11] Therefore, these changes alone are not particularly useful for diagnosing osteoporosis. In light of the complexity in the articular x-ray signs of osteofluorosis, when diagnosing osteoporosis using x-rays, determination should be made using all the various signs in tandem; this will help improve accuracy and reliability of the final diagnosis.[12-13]

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