

Dr. Burk: What you say is true, but by taking the ten largest cities in each group throughout the United States, these factors tend to be equalized. With such large numbers of people involved it is highly unlikely that there would be appreciable differences in such factors as smoking habits or even the amount and effects of air pollution.

FLUORIDE-INDUCED CHANGES IN 60 RETIRED ALUMINUM WORKERS

by

E. Czerwinski and W. Lankosz
Cracow, Poland

SUMMARY: Orthopedic, radiological and analytical examinations were performed in a group of 60 retired disabled workers of an aluminum factory. Occupational disease had previously been recognized in this group because of disturbances in the respiratory and circulatory systems. The age of those examined averaged 49.6 years; the duration of exposure averaged 16.9 years; 88.3% had worked in the electrolysis department.

In the majority of cases orthopedic examination showed changes of a generalized character in locomotion, differing in the degree of intensity. Exostoses and ossification of the interosseous membranes and muscle attachments were the most frequently detected radiological changes. Generalized sclerosis and periosteal reactions occurred less frequently. No major variations from the norm were noted in the levels of serum calcium, phosphorus, acid and alkaline phosphatase.

Expansion of the industrial uses of fluoride compounds accounts for an ever-increasing pollution of the environment. The halogen emanates into the environment during industrial exploitation of minerals containing fluoride (cryolites, apatites, phosphorites) in aluminum and fertilizer factor-

From the Orthopedic Department, Academy of Medicine. Head: Doc. dr hab Janina Markowa, Cracow, Poland.

ies. Fluoride compounds, emitted during electrolysis and other processes using the above-mentioned minerals, are absorbed by the lungs and by the digestive tract whence they are promptly transported to the circulatory system (1-3). About 60% of a given dose is excreted with the urine, but almost 90% of what remains accumulates in bones (3-5) due to the affinity of fluoride for hydroxyapatite, the basic mineral substance of bone. Fluoride exchanges the hydroxyl ion of hydroxyapatite to fluoroapatite, which is much less soluble than hydroxyapatite (6, 7). At the same time fluoride affects the activity of parathormone, calcitonin, and the acid and alkaline phosphatases. Reduction in the solubility of the bone apatite crystals together with the hormone changes leads to a positive calcium balance and to the predominance of osteogenesis (6-11).

The morbid changes of chronic, excessive fluoride intake are known as fluorosis which occurs either in the form of industrial fluorosis in workers exposed to fluoride compounds or as endemic fluorosis in regions with a high fluoride content naturally in drinking water (1-2, 12-18). The clinical picture of industrial fluorosis consists of changes in the respiratory, circulatory and digestive systems, in dental and neurological abnormalities and in changes in bones and joints (2, 12, 14, 19-24). Locomotor changes due to great variations in temperature, humidity and mechanical stress during work hours often occur in foundry workers, especially in aluminum smelters where exposure to fluoride may be a health hazard.

This study will evaluate fluorotic changes in a group of 60 retired disabled workers of an aluminum factory.

Method and Material

In the 60 retired workers occupational disease had previously been diagnosed on the basis of changes in the respiratory-circulatory system. Their ages ranged from 37 to 69 (average 49.6). They had been working in the aluminum factory from 10 to 29 years (average 16.9). Fifty-three had previously worked in the electrolysis department, including 32 electrolysis operators, 7 anode operators, 14 at other jobs in the same department; 7 subjects had been employed in other departments.

All retired disabled workers underwent orthopedic check-ups and x-rays of the lumbar spine, pelvis and forearms. Radiograms of other parts of the skeleton were taken in selected cases. Levels of serum calcium, phosphorus, acid and alkaline phosphatase were determined, as well as the fluoride levels in the urine. In one case the fluoride content of a bone sample was estimated.

Results

I. Clinical Changes in Bones and Joints: In the majority of cases orthopedic examination showed generalized changes in locomotion of various degrees of intensity. Most often the patients complained of back pain. Pains in the shoulders, elbows, forearms and lower legs were common. These pains differed in intensity and occurred constantly or periodically with no clear relationship to effort. Upon examination, we found limited mobility in the joints of the spine and extremities, ranging from a trivial to a marked decrease in the range of movements.

In the spine, we most frequently found limitation of movements in the lumbar and thoracic region, but rarely in the cervical spine. In a few cases the spine was ankylosed. In 15 patients we found disturbances in the spinal column in the form of dorsal kyphosis and lumbar scoliosis. Marked restriction of the respiratory movements of the chest was also encountered. The average difference in chest circumference at maximal inspiration and expiration was 2.5 cm.

In the extremities, limitation in the rotatory movements of the forearms, shoulders and hip joints occurred most frequently, while limitation of movements on the sagittal plane was noted less often. In about

Table 1
Clinical Changes in Bones and Joints

<u>Symptoms</u>	<u>Frequency of Occurrence</u>	
<u>Pain in joints</u>	<u>90%</u>	
back		78%
shoulder		63%
knee		43%
hip		38%
elbow		31%
<u>Limitation in range of movements</u>	<u>68%</u>	
rotation of forearms		67%
movements of spine		63%
movements of hip		43%
movements of shoulder		36%
movements of elbow		27%
movements of knee		25%
<u>Crepitation during movement</u>	<u>42%</u>	

half the cases we observed crepitation in the joints during movements, especially in the knee joints.

The painful symptoms reported did not always correspond to the limitation in the joint mobility, since we also found limitation of movement in joints without pain. The clinical changes in locomotion are summarized in Table 1.

II. Radiological Changes in the Skeleton: An evaluation of radiograms of the lumbar spine, pelvis, forearms and lower legs is presented in Table 2. A common finding in the radiogram was marginal exostoses of the

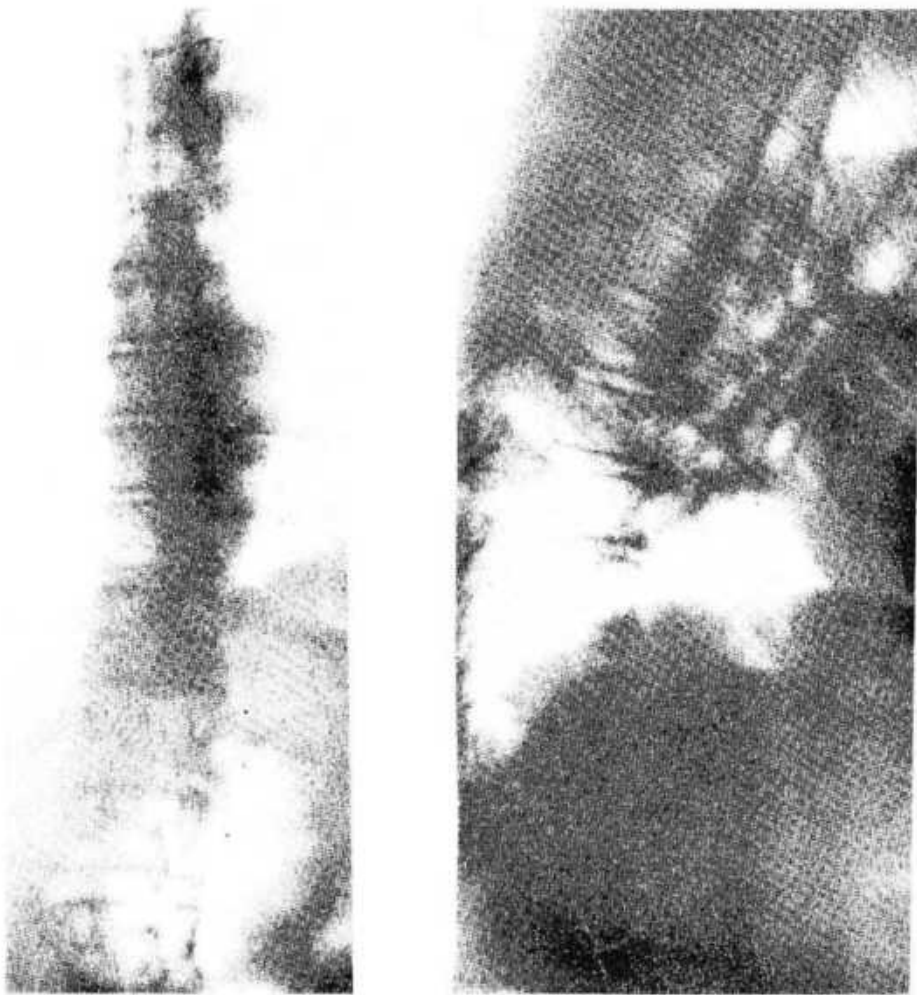
Table 2
Radiological Changes in the Skeleton

<u>Symptoms</u>	<u>Frequency</u>	
Ossification of ligaments and muscle attachments, and exostoses	97%	
spine		95%
pelvis		93%
forearms		58%
lower legs		57%
Lumbar scoliosis	45%	
Congenital spinal defects	28%	
Ossification of joint capsules	65%	
hip		55%
knee		25%
elbow		15%
Free intra-articular bodies	48%	
Ossification of pubic symphysis	54%	
Blurring of outline of sacro-iliac joints	32%	
Ossification of interosseous membranes	97%	
forearms		97%
lower legs		57%
Periosteal bone appositions	68%	
forearms		68%
lower legs		53%
Thickening of cortical bone	87%	
forearms		73%
lower legs		67%
Thickening of acetabulum bottom		54%
Alteration of bone structure		
Osteo-	66%	
sclerosis		
pelvis		47%
spine		41%
Resorption	8%	
forearms		6%
spine		4%
pelvis		2%

vertebral corpora and ossifications of the longitudinal ligaments and annular fibrosis, leading to the formation of osseous bridges between adjoining vertebrae (Figure 1). In the patients with lumbar scoliosis the changes described were more advanced (Figure 2). Congenital defects of the sacro-lumbar area such as spina bifida, sacralization of L₅ and lumbarization of S₁ were found in 15 patients.

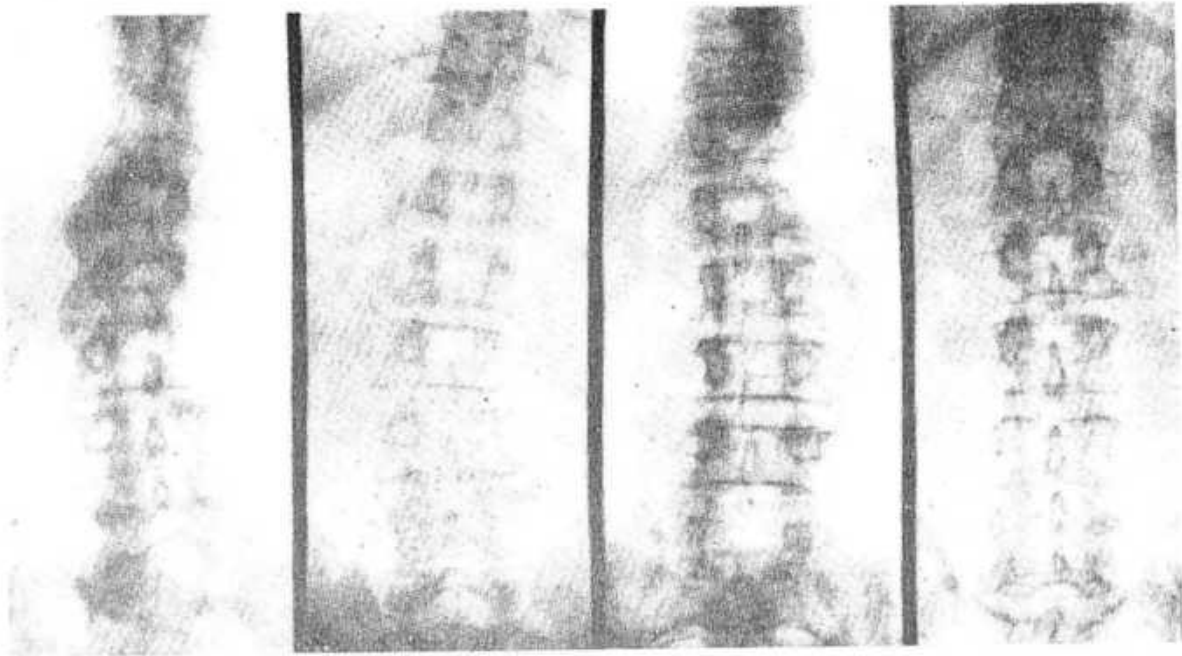
The radiological changes in the pelvis included ossification of the muscle attachments of the iliac bone, the ramus of the ischiac bone and the pelvic ligaments. In the radiogram of the pelvis ossification of joint capsules, free intra-articular bodies, and obliteration of the sacro-iliac joint spaces were found.

Figure 1
Fluorotic Change in the Spine of an
Aluminum Worker Aged 42



Marginal exostoses on the anterior and posterior surfaces of the vertebral bodies, slight osteosclerosis, thoracic kyposis and lumbar scoliosis.

Figure 2
Different Degrees of Osteosclerosis of the Lumbar Spine



Advanced degenerative changes and disturbances in the lumbar spinal statics.

In all cases the radiograms of the forearm and lower leg showed ossification of the interosseous membranes. Ossification of the capsules of the elbow and knee joint and free intra-articular bodies occurred more rarely. Thickening of the cortical bone at the diaphysis was noted frequently and ranged from a small degree up to complete closure of the medullary cavity.

Bone Structure: In the x-ray evaluation, special attention was paid to a marked increase in the patterns of the bone structure. Half the cases examined showed a distinctive and marked density of the bone shadow together with a thickening of the trabeculation to the point of complete disappearance of the latter. It should be pointed out that we diagnosed osteosclerosis on the basis of visual comparison of the radiogram with the picture normally encountered and accepted its existence only in cases which were free of any doubt. More precise evaluation would be possible only after performing densimetric analysis.

A few cases showed disturbances in the trabecular structure besides osteosclerosis in the form of dispersion and in addition mottled osteosclerosis of the substantia spongiosa as well as endosteal bone resorption.

III. Other Changes : In all patients respiratory-circulatory symptoms occurred which were the main cause qualifying them for a disability pension. Only a few cases were qualified for a disability pension due to other diseases. Thirty of those examined suffered from diseases of the alimentary tract, such as dyspepsia or gastritis. Gastric or duodenal ulcers occurred in 7 (or 12%) of those examined, 5 of whom (8%) had undergone gastric resection.

The majority of cases exhibited dental changes such as a tendency to abrasion, fragility, etc. Cholelithiasis and urolithiasis occurred in 13% of cases. As many as 23% suffered from psychiatric disturbances such as depression, mental sluggishness, or memory disturbances. The frequency of non-locomotor changes is presented in Table 3.

Table 3
Non-skeletal Changes

<u>Manifestations</u>	<u>Frequency of Occurrence</u>
Respiratory and circulatory system	97%
Digestive system	51%
Gastric ulcer	12%
Status after stomach resection	8%
Urolithiasis and cholelithiasis	13%
Dental changes	74%
Psychiatric disturbances	23%

IV. Additional Tests: The fluoride levels in the urine were markedly elevated in all cases. No appreciable abnormal variations were noted in the serum calcium, phosphorus or alkaline and acid phosphatase levels. A detailed analysis of the additional tests will be presented separately. The fluoride level in a bone sample from the iliac crest in one case was 120 mg% in the fat-free bone ash (25).

A comparison of the frequency of occurrence of changes in bones and joints in workers with various degrees of exposure to fluoride compounds (electrolyser operators and others from the same and other departments) is presented in Table 4 and the frequency of changes in both groups as related to the length of employment (10-15 years or 16-20 years) in Table 5.

Table 6 shows the relationship of the changes to the age of those examined in the age-groups under 50, 51-60, and above 60. The frequency of changes in retired workers does not depend on the place of work or the position, but on the length of employment. Those who had worked longer and the older age groups showed greater changes in locomotion.

Table 4
Relation of Changes in Bones and Joints to the Jobs

Symptoms	Electrolysis Department			Other Departments	Total
	electrol. operator	anode operator	others		
	32	7	14	7	
Joint pains	97%	71%	86%	86%	90%
Limitation of movements	75%	57%	57%	71%	68%
Disturbances in spinal column (clinical and radiological)	56%	71%	50%	43%	55%
Ossification of muscle attachments, exostoses	97%	86%	100%	100%	97%
Ossification of interosseous membranes	97%	86%	100%	100%	97%
Periosteal bone appositions	63%	71%	86%	57%	68%

Table 5
Changes in Bones and Joints Related to Duration of Exposure

Symptoms	10-15 years	16-20 years	Total
	14 cases	46 cases	60 cases
Joint pains	71%	96%	90%
Limitation of movements	57%	72%	68%
Disturbances of spinal column (clinical and radiological)	57%	54%	55%
Ossification of muscle attachments, exostoses	86%	100%	97%
Ossification of interosseous membranes	100%	93%	97%
Periosteal bone appositions	57%	72%	68%

Table 6
Relation of Changes to Age

Symptoms	under 50 years	51-60 years	over 60 years	Total
	28 cases	20 cases	12 cases	
	Joint pains	90%	86%	
Limitation of movements	46%	86%	75%	68%
Disturbances of spinal column (clinical and radiological)	50%	55%	67%	55%
Ossification of muscle attachments, exostoses	96%	95%	100%	97%
Ossification of interosseous membranes	96%	95%	100%	97%
Periosteal bone appositions	58%	75%	83%	68%

Discussion

The clinical and radiological findings in the group investigated correspond to the picture of industrial fluorosis described by others (1-2, 12-14, 17, 19, 21-24, 26). Complaints of pain and limitations in joint movements are less characteristic features than the changes shown in radiograms.

Typical fluorotic changes in the radiogram are generalized osteosclerosis, periosteal reactions, and ossification of the interosseous membranes and muscle attachments (1-2, 12, 14, 17, 19-20, 24). Less characteristic but commonly occurring in the radiogram of the lumbar spine are exostoses and ossification of ligaments, presenting the radiological picture of spondyloarthrosis or spondylitis ankylopoetica (19, 21-22, 27-28).

The part played by fluoride in degenerative changes in the spine and joints has not yet been elucidated. Fradà, Vischer and Andreyeva reported the frequent occurrence of degenerative changes in subjects exposed to fluoride compounds, but Zipkin and Steinberg found no relation between the action of fluoride and degenerative changes (7, 15, 21, 29-30).

In our material we noted degenerative changes in the lumbar spine in 95% of cases, which suggests that fluoride accelerates these changes. In addition to pain in the lower spine which is associated with radiological changes, patients with negative x-ray findings also complain of pain in the lumbar-sacral area, an indication that symptoms precede changes demonstrable by x-ray (2, 31-33). In our subjects radiological changes, especially ossification of the interosseous membrane, were found in patients who had not reported any painful symptoms.

In the group studied, radiological findings were present in 96% of cases. Such a high incidence of changes is undoubtedly the result of selection of the group examined. Occupational disease was diagnosed in all cases; all were employed for over 10 years. According to Roholm (17) initial bone changes occur after 2.5 - 4 years but according to Andreyeva they are rare before 9 - 10 years of work (12). The frequency of appearance of radiological changes in aluminum workers has been evaluated by different authors: Andreyeva noted 33%, Fradà 10%, Gotlib 9.5% (12, 14, 21). In a selected group of workers with long employment Vischer reported changes in 86% of cases (2).

We have not found that elbow joints, especially the right ones are more often affected than others as reported by Fradà and Vischer (2, 14) nor have we seen any essential differences in the radiograms of a group of workers periodically using percussion tools as compared with other groups.

Respiratory-circulatory and digestive symptoms, dental and neuromuscular changes in locomotion found in the cases show that chronic fluoride intoxication involves the entire human body and is not confined to teeth and bones as pointed out by Waldbott (34).

Conclusions

1. Pathological changes in locomotion were found in all sixty retired aluminum workers.
2. These changes were of a generalized character manifesting pains in joints and limitation in movements of differing intensity.
3. Radiograms showed most frequently ossification of the interosseous membranes and muscle attachments, as well as exostoses. Ossification of the joint capsules, free intra-articular bodies or generalized osteosclerosis were found less often.
4. Changes in the bones and joints occurred more frequently in workers who had retired after a long period of employment and in the elderly. The position held did not affect the frequency of occurrence of changes.
5. Bone changes in the radiogram are a valuable criterion in the diagnosis of fluorosis.
6. Workers in aluminum factories should undergo regular prophylactic x-ray examinations.

Acknowledgements

This work was partly supported by the Committee for Medical Sciences of the Polish Academy of Science. Fluoride assays were carried out in the Department of Analytical Chemistry of the Cracow Academy of Medicine (Head: Doc. dr hab. Jan Sznajd.) and at the Cracow Institute of Forensic Expertise (Head: Doc. dr hab. J. Markiewicz).

Bibliography

1. Martin, A.E.: Industrial Fluoride Hazards. Fluoride and Human Hlth., 310-316, WHO, Geneva, 1970.
2. Vischer, T.L., Bernhein, C., Gudjikoff, C., Wettstein, P.P., and Largier, R.: Industrial Fluorosis. Fluoride in Medicine, 96-105, Hans Huber Publishers, Bern, 1970.

3. Wallace - Durbin, P.: The Metabolism of Fluoride in the Rat using F-18 as a Tracer. *J. Dent. Res.*, 11:789-800, 1954.
4. Ahrens, G.: The Excretion of Fluoride by Osteoporotic Patients Under Sodium Fluoride Therapy. *Fluoride in Medicine*, 175-177, Hans Huber Publishers, Bern, 1970.
5. Hein, J.W.: Distribution in the Soft Tissue of the Rat of Radioactive Fluoride Administered as Sodium Fluoride. *Nature*, 178:1295-1298, 1956.
6. Baylink, D.: Effect of Fluoride on Bone Formation, Mineralization and Resorption in the Rat. *Fluoride in Medicine*, 37-69, Hans Huber Publishers, Bern, 1970.
7. Gedalia, I., Zipkin, I.: The Role of Fluoride in Bone Structure. *Israel J. of Medical Science*, No. 72-878224, Jerusalem, 1973.
8. Messer, H.H., Armstrong, W.D., Singer, L.: Fluoride, Parathyroid Hormone and Calcitonin: Effects on Metabolic Processes Involved in Bone Resorption. *Calc. Tissue Res.*, 13:227-233, 1973.
9. Messer, H.H., Armstrong, W.D., Singer, L.: Fluoride, Parathyroid Hormone and Calcitonin: Inter-relationship in Bone Calcium Metabolism. *Calc. Tiss. Res.*, 13:217-225, 1973.
10. Reutter, W.F., Siebenman, R.: Fluoride in Osteoporosis. In *Fluoride in Medicine*. Vischer, T.L., Ed., Hans Huber, Bern, 1970, pp. 143-152.
11. Teotia, S.P.S., Teotia, M.: Hyperactivity of Parathyroid Glands in Endemic Osteofluorosis. *Fluoride*, 3:115-125, 1972.
12. Andreyeva, T.D., Girskaia, E.Y.: Radiological Diagnosis of Bone Changes in Workers with Fluorosis from Cryolite and Aluminum Plants. *Voprosy Gigieny i Profiessyonalnoy Patologii v Tsvietnoy i Chernoy Metallurgii*, Sverdlovsk, 1971, pp. 52-54.
13. Bhussry, B.R., Demole, V., Hodge, H.L., Jolly, S.S., Singh, A. and Taves, P.R.: Toxic Effects of Larger Doses of Fluoride. *Fluorides and Human Health*, W.H.O., Geneva, 1970, pp. 225-265.
14. Fradà, G. and Montesana, G.: The Clinical Features of Hydrofluorosis. *Pan minerva Medica*, 8:50-57, 1966.
15. Johnson, C.L., Smith, F.A.: *Fluoride Chemistry*. vol. IV, Academic Press, New York and London, 1965.
16. Jolly, S.S.: Hydric Fluorosis in Punjab. *Fluoride in Medicine*, 106-21, Hans Huber Publishers, Bern, 1970.
17. Roholm, K.: *Fluoride Intoxication*. H.K. Lewis, London, 1937.
18. Teotia, M. and Teotia, S.P.S.: Further Observations on Endemic Fluoride-Induced Osteopathies in Children. *Fluoride*, 3:143-151, 1973.
19. Franke, J.: Die Knochenfluorose. *Therapie Woche*, 23-43, 3954, 1973.
20. Gorzkowski, E., Domanski, Z., Jelonek, W., Neuman, Z. and Szymkowitz, M.: Ogólny stan zdrowia pracowników zakładów nawozów fosforowych. Wybrane zagadnienia toksykologii przemysłowej związków fluoru.

- 23-26. Poznańskie Towarzystwo Naukowe, Szczecin-Poznań, 1871.
21. Gotlib, E. V., Simahina, P. G., Miller, S. V., Zislin, D. N., Girskaia, E. Y. and Andreyeva, T. D.: Occupational Pathology in Workers from Electrolysis Departments of Aluminum Plants. In no. 12, pp. 33-37.
 22. Grinberg, A. V., Orlovska, T. V., Ornican, E. Y. and Sagotov, I. S.: The Early X-Ray Diagnosis of Fluorosis. In no. 12, pp. 49-51.
 23. Gubanov, E. N.: Dental Changes in Workers from Electrolysis Departments of Aluminum Plants. In no. 12, pp. 44-46.
 24. Tzonchev, V., Seidel, K., Dimitrov, M.: The Radiology of Joint Diseases. Butterworth and Co., 1973.
 25. Klewska, A.: Application of Microdiffusion Technique to the Determination of Fluoride in Biological Material. Arch. Med. Sad. i Krym., 13:279-283, 1973.
 26. Waldbott, G. L. and Ceciloni, V. A.: "Neighborhood" Fluorosis. Fluoride, 2:287-396, 1969.
 27. Borejko, M., Dziak, A.: Radiological Examination in Orthopaedics. PZWL, Warsaw, 1973, pp. 1-11 and 221-230.
 28. Bruhl, W.: The Disease of the Locomotor System. PZWL Warsaw, 1969, pp. 413-433.
 29. Steinberg, C. L., Gardner, D. E., Smith, F. A. and Hodge, H. C.: Comparison of Rheumatoid (ankylosing) Spondylitis and Crippling Fluorosis. Ann. Rheum. Dis., 14:378, 1955.
 30. Zipkin, I., Sokoloff, L., Frazier, P. D.: A Study of the Effect of Fluoride on Bone and Osteoarthritis in Mice. Isr. J. Med. Science, 3: 719, 1967.
 31. Cook, H. A.: Crippling Arthritis Related to Fluoride Intake. Fluoride, 4:209-213, 1972.
 32. Steinberg, C. L., Gardner, D. E., Smith, F. A. and Hodge, H. C.: Fluoridation of Public Water Supplies and its Relation to Musculoskeletal Diseases. N. Engl. J. Med., 258-322, 1958.
 33. Waldbott, G. L.: Incipient Chronic Fluoride Intoxication from Drinking Water I. Report on 52 Cases. Acta Medica Scand., 156:157-168, 1956.
 34. Waldbott, G. L.: Introduction, Symposium on the Non-Skeletal Phase of Chronic Fluorosis. Fluoride, 9:5-8, 1976.

Discussion

Dr. Waldbott: I consider Dr. Czerwinski's paper very important, as he has described the same symptoms in industrial fluorosis that I have observed in incipient poisoning from fluoridated water. Thus my observations on preskeletal fluorosis are being confirmed.