COMPARISON OF RHEUMATOID (ANKYLOSING) SPONDYLITIS AND CRIPPLING FLUOROSIS*†

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Crippling fluorosis and rheumatoid (ankylosing) spondylitis present a confusing similarity; both are

characterized in their advanced stages by a "poker-back" spine with calcification of the ligaments of the spinal column (Fig. 1). Rheumatic pains of various degree are common in the early stages of both diseases.

One of us (C.L.S.), noting the similarity between

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Fig. 1.—"Poker Back", comparison of limitation of motion and characteristic stance in (A and B) rheumatoid spondylitis, and (C and D) crippling fluorosis. C and D are reproduced with the permission of the publishers from Roholm (1937, opp. p. 145, Figs 33b and c).

these conditions, suggested the importance of presenting a comparison of the two conditions. Recent public health undertakings in the United States, designed to reduce the incidence of dental caries by adding fluoride to the communal water supply, have increased the importance of this investigation. It would be unfortunate if these undertakings were erroneously accused of producing serious bone changes through the inadvertent diagnosis of rheumatoid (ankylosing) spondylitis as crippling fluorosis.

Rheumatoid (Ankylosing) Spondylitis

This condition is usually considered by most rheumatologists to be a variant of rheumatoid arthritis. It usually affects males in contradistinction to the usual variety of rheumatoid arthritis which generally affects females. It usually begins in youth, is characterized by exacerbations and remissions of back pain, and may or may not be associated with the sciatic syndrome. As the disease progresses a gradual stiffening of the back occurs, eventually resulting in a "poker-back" spine. Expansion of the chest on inspiration becomes diminished and finally nil as ankylosis of the costovertebral joint occurs. The radiographic picture is pathognomonic. The first changes usually occur in the sacro-iliac joints. The joint surface becomes irregular; there is progressive increase in density in the contiguous bone surfaces of this joint. Eventually the sacro-iliac joints may be completely obliterated by bony ankylosis. At this particular point the area in which the joint has been erased is usually very dense; the surrounding bone area may show a decrease in density. The trabeculae become more prominent. Calcification occurs in the anterior and longitudinal ligaments of the vertebral column. However, there is no calcification in the sacral tuberosus and other ligaments of the pelvis, nor are the fasciae involved. Primary fibrous and subsequent bony ankyloses of the apophyseal joints result in a rigid spinal column ("poker-back" spine). Approximately 25 per cent. of these patients have involvement of the peripheral joints with a clinical pattern not unlike rheumatoid arthritis. The sedimentation rate is elevated in a majority of the cases.

Crippling Fluorosis

Crippling fluorosis is a specific form of skeletal disease which follows the absorption of excessive amounts of fluoride for prolonged periods of time. Osteosclerosis and exostoses are the outstanding findings; mottled dental enamel may be seen if the period of *absorption* includes the first 8 years of life when the enamel of the permanent teeth is being

formed. In some instances areas of osteoporosis also are seen. As the disease progresses all bones eventually become sclerotic; there seems to be a predilection, however, for flat bones, such as those of the pelvis and jaw, and especially the lumbar vertebral system to show the first detectable changes (Felson, 1955). In severe cases, exostoses become evident on the long bones, and on the lower edges of the vertebrae. Eventually the vertebrae fuse together, the spinal ligaments become calcified at their points of attachment, and the typical rigid spinal column ensues (Figs 2, 3, and 4, overleaf). Crippling fluorosis of industrial origin was fully described by Roholm (1937) in his investigation of the disease in Danish cryolite workers. The condition is also endemic in various parts of the world, India, China, Argentina, and South Africa, where water supplies contain 2-16 parts per million of fluoride. From data presented by McClure (1943), fluoride doses probably must be greater than 0.1 mg./kg./day during the first 8 years of life to produce mottled enamel. It has been estimated that the daily consumption of 0.3-1.0 mg. fluoride per kg. body weight for a period of 10-20 years will result in crippling fluorosis (Roholm, 1937; Hodge and Smith, 1954).

Present Investigation

To our knowledge no one has reported the fluoride content in the skeletal tissues of an individual suffering from rheumatoid spondylitis. It was our unusual fortune recently to study such a case; this man who had had the disease for a period of 10 years died suddenly of a subarachnoid haemorrhage.

Case History

A white male aged 40 years, first seen on September 22, 1948, gave a 10-year history of low back pain with progressive spinal stiffening, and increased pain and stiffness of the hips. He had lived in Rochester, N.Y., all his life, and never had left the area for any period longer than a few days. The fluoride content of the tap water by analyses in the period 1945 to 1952 was low, about 0.06 parts per million; presumably this is a reliable estimate of the fluoride content of Rochester's water supply during the man's life time.

The physical examination revealed no dental mottling. He lacked 15° abduction in both shoulders; there was no chest expansion on deep inspiration, which was thought to be indicative of ankylosis of the costovertebral joints. He was unable to abduct either hip, and a 45° flexion deformity was present in both. His entire spine was rigid.

Laboratory Findings.—September 22, 1948:

Antistreptolysin titre, 83 units; red blood cells, 4,530,000; haemoglobin, 12 g. per cent.; white blood cells, 13,600.

Fig. 2.—Moderately advanced crippling fluorosis in male, lumbo-sacral area. Note increased bone density (sclerosis) and loss of normal trabecular pattern.

Fig. 4.—Advanced crippling fluorosis, lumbo-sacral area. Advanced calcification of ligaments (arrows). Marked increase in bone sclerosis appears to "obliterate" normal sacro-iliac joints.

Fig. 3.—Advanced crippling fluorosis, lumbo-sacral area. Note complete loss of bone trabecular pattern and "marble" type bone due to increased bone sclerosis. Moderate calcification of ligaments.

Differential Blood Count: stabs, 2 per unit; segmented neutrophils, 78 per cent.; lymphocytes, 10 per cent.; eosinophils, 3 per cent.; monocytes, 7 per unit; blood uric acid, 1.6; serum calcium, 10.4; serum phosphorus, 3.9 mg. per cent.; erythrocyte sedimentation rate, 35 mm./hr (Wintrobe-Landsberg). Subsequent sedimentation rates varied between 21 and 39 mm. Bone marrow fat 3, plasma 48, erythromyeloid layer 9, haematocrit 40 vol. per cent. The marrow showed no abnormalities.

Radiographs (September 22, 1948).—Anterior-posterior stereo and lateral films of the cervical spine (Fig. 5, opposite) showed calcification in the anterior vertebral ligaments. In addition there was evidence of bony sclerosis or ligamentous calcification along the posterior portion of the articular facet in the lower cervical region. The cervical bodies and intervertebral spaces appeared to be normal.

In the thoracic spine moderate scoliosis was seen with a major curve at the lumbo-dorsal region with the convexity on the left side. There was evidence of mild osteoporosis involving the thoracic segments, but no other definite changes.

The lumbar spine and pelvis (Figs 6 and 7, opposite) showed advanced ligamentous calcification along the anterior borders of the lower lumbar vertebral bodies

Fig. 5.—Rheumatoid spondylitis, lateral view of cervical spine. Note bony ankylosis of apophyseal joints.

Fig. 6.—Rheumatoid spondylitis, lateral view of lumbo-sacral area. Note calcification of anterior spinal ligament.

and suspected calcification in the posterior ligaments. There was no evidence of bony sclerosis in the sacro-iliac region on either side, but there was evidence of destructive arthritic change involving both hips with irregularity of the femoral head and acetabulum. Ligamentous calcification was seen inferiorly about both hip joints.

Treatment.—A left cup arthroplasty was done on January 14, 1949. There was slight irregular new bone formation in an area where the cartilage was denuded. The periosteum was thickened irregularly.

A right cup arthroplasty was done on May 9, 1949. The microscopic sections revealed a markedly proliferative synovial tissue with foci of inflammatory cells beneath the mesothelium. The bone tissue was essentially normal.

Death.—On May 13, 1952, the patient died suddenly of a subarachnoid haemorrhage.

Autopsy.—Portions of the ribs, vertebrae, and sacrum and ilium immediately adjacent to the sacro-iliac joint were taken for fluoride analysis. The soft tissue adhering to each of the specimens and marrow from the two rib specimens were analysed separately. The vertebral sample was separated into the spongy and dense portions, (Fig. 8, overleaf). The soft tissues were analysed according to the method described by Smith and Gardner (1951) for blood fluoride. After ashing the hard tissues, fluoride was separated by the perchloric acid distillation of Willard and Winter (1933); fluoride in the distillate was determined by salt-acid thorium titration (Smith and Gardner, 1950). The data obtained are shown in Table I (overleaf).

Fig. 7.—Rheumatoid spondylitis, anterior-posterior view of pelvis. Note ankylosis of sacro-iliac joints and increased trabeculation of bone.

Fig. 8.—Separation of vertebral sample from a case of rheumatoid spondylitis for fluoride analysis: (a) spongy portion, 410 p.p.m. fluoride in ash; (b) soft tissue, 17 p.p.m. fluoride fresh wt.; (c) dense portion, 310 p.p.m. fluoride in ash.

TABLE I
FLUORIDE CONCENTRATIONS IN TISSUES

Site of Tissue	Fluoride (parts per million)	
	in Ash	in Fresh Tissue
Rheumatoid Spondylitis Patient	Ilium	320
	Sacrum	310
	Soft tissue between sacrum and ilium	9
	Smaller rib including marrow	420
	Smaller rib without marrow	440
	Smaller rib marrow	17
	Soft tissue around smaller rib	10
	Larger rib including marrow	420
	Larger rib without marrow	440
	Larger rib marrow	10
Controls*	Soft tissue around larger rib	9
	Vertebra, spongy portion	410
	Soft tissue from vertebra	17
	Vertebra, dense portion	310
Controls*	Rib	405-1,215
	Soft tissue around rib	9-21
	Rib marrow	26
Controls*	Vertebra	440-1,320
	Soft tissue round vertebra	7-20

* Smith, Gardner, and Hodge, 1955.

There were no known opportunities for this patient to have been exposed to excessive amounts of fluoride. Nevertheless, the fluoride content of bone samples, which are shown to be normal, conclusively rule out fluorosis as a factor in the disease.

Discussion

Fluoride is a normal trace constituent of bone, the contents depending on the fluoride intake, the age of the individual, and probably on other factors. Rib and vertebral specimens from 40 to 50-year-old male residents of the Rochester area contained 400 to 1,300 p.p.m. fluoride in the ash (Smith, Gardner, and Hodge, 1955). Martin (1948) has reported similar fluoride concentrations in dry defatted samples from the crest of the ilium obtained in Evanston, Illinois, prior to water fluoridation; using the data of Robinson (1952) for fat content, these adult bones were calculated to contain 470 to 1,430 p.p.m. fluoride in the ash.

The data in Table I show that the tissues of the ribs of our patient contained low but normal amounts of fluoride, whereas the vertebrae contained slightly less fluoride than had been found in control patients of the same age (Smith, Gardner and Hodge, 1953). The ilium also contained slightly less fluoride than Martin (1948) reported for a series of nine samples of the iliac crest.

Soft tissues contain normally only traces of fluoride; the finding that fluoride concentrations in the soft tissues and marrow (9 to 17 p.p.m.) were much lower than those found for the hard tissues was expected. Concentrations found for comparable tissues from five patients without rheumatoid spondylitis, 14 to 86 years of age, averaged 9 to 26 p.p.m.

The data obtained in this study indicate that the increased osteosclerosis encountered in rheumatoid spondylitis is not associated with increased skeletal

TABLE II
FLUORIDE CONCENTRATIONS IN BONE

Site	Fluoride (parts per million)		
	Normal*	Rheumatoid Spondylitis	Crippling Fluorosis†
Rib	405-1,215	420-440	9,900-11,200
Vertebra	440-1,320	310-410	9,300-13,100

* Smith and others (1953).

† Roholm (1937), p. 193.

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TABLE III

COMPARISON OF RHEUMATOID SPONDYLITIS, CRIPPLING FLUOROSIS, AND METASTATIC CARCINOMA

Condition	Rheumatoid Spondylitis	Crippling Fluorosis	Metastatic Carcinoma (Prostate and Breast)
(1)	Increase in trabecular pattern upon roentgenological examination	Coarse and blurred trabeculae, diffuse increased density of bone on roentgenological examination	Localized areas of increased bone density
(2)	Increased density of sacro-iliac joints and increased density of ilium and sacrum with progressive disease	Vertebral system and pelvis affected first and most severely; later extended to ribs and extremities. All bones are affected, particularly cancellous bones. Exostoses on long bones	Pelvic area and lumbar spine affected first. Areas of increased bone density usually discrete, but occasionally diffuse. No cortical thickening
(3)	Universal occurrence	Endemic where water supplies contain excessive amounts of fluoride. Formerly seen in workers handling fluoride-containing compounds	Universal occurrence
(4)	Calcification of ligaments limited to anterior and lateral spinal column	Excessive calcification of tendons, ligaments, fasciae	No ligamentous calcification
(5)	Peripheral joints swollen in 25 per cent. of cases	Bones of extremities thickened	No peripheral joint involvement
(6)	No mottled enamel	Mottled enamel may be present if fluoride exposure excessive during period of formation of enamel of permanent teeth	No mottled enamel
(7)*	No increased urinary fluoride excretion	Urinary excretion of fluoride increased	No increase in urinary fluoride excretion
(8)†	Skeletal fluoride concentration not increased	Increase in skeletal fluoride concentration	No increase in skeletal fluoride concentration
(9)	No increase in serum phosphatase	No increase in serum phosphatase	Increase in serum alkaline, acid phosphatase, or both

* When the fluoride concentration in the urine is consistently less than 5 mg./l., no roentgenographically demonstrable osteo-sclerosis develops (Irwin, 1954).

† Normal concentration of fluoride in human bone (Smith, Gardner, and Hodge, 1955, unpublished data):

Sex	Site	Age	P.p.m.
Male	Rib	10	300
		90	1,480
	Vertebrae	10	380
		90	1,520
Female	Rib	10	240
		90	1,200
	Vertebrae	10	320
		90	1,260

deposition of fluoride. Indeed, the skeletal fluoride concentrations were near or less than the normal limits previously established. Fluoride cannot be held responsible for the bony changes in rheumatoid spondylitis. Roholm (1937) has shown that the skeletal tissues of patients disabled with fluorosis contain relatively high concentrations of fluoride. Representative data for rib and vertebra are shown in Table II. Wolff and Bauer (1938) reported greatly decreased fluoride concentrations in occipital, parietal, and frontal bones in a series of six cases of Paget's disease (osteitis deformans).

A comparison of rheumatoid spondylitis, crippling

fluorosis, and metastatic carcinoma is presented in Table III. The data on metastatic carcinoma are included because the increased x-ray density of certain lumbar vertebrae has presented a problem in differential diagnosis.

Summary

(1) Fluoride concentrations were determined for autopsy samples of rib, sacrum, ilium, vertebra, adhering soft tissue, and rib marrow from a patient suffering from rheumatoid (ankylosing) spondylitis of 10 years' duration. The fluoride concentrations were not increased above normal levels. In this case, the increased bone density seen in this disease was not the result of increased skeletal fluoride deposition.

(2) A tabular comparison of rheumatoid spondylitis, crippling fluorosis, and metastatic carcinoma is presented.

Dr. Robert A. Robinson, formerly of the Division of Orthopaedic Surgery, of the University of Rochester School of Medicine and Dentistry, gave us a number of valuable suggestions and assisted in preparing the samples of sacrum and ilium for analysis. The Department of Medical Photography, Rochester General Hospital, prepared Figs 5-7. Mr. Leon Schwartz of the Photo-

graphy Section, University of Rochester Atomic Energy Project, prepared the diagram Fig. 8. Mr. Fred Brandlin, formerly of the Industrial Hygiene Section, University of Rochester Atomic Energy Project, prepared the x-ray shown in Fig. 8.

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Comparaison de la spondylite rhumatismale et de la fluorose mutilante

RÉSUMÉ

(1) On a déterminé le taux de fluor dans les pièces d'autopsie provenant des côtes, du sacrum, de l'os

iliaque, des vertèbres, des tissus mous adhérents et de la moelle costale d'un sujet ayant souffert de spondylite rhumatisante pendant dix ans. Le taux de fluor n'était pas au dessus de la normale. Dans ce cas donc la condensation osseuse habituelle dans cette maladie ne pouvait pas être attribuée à l'augmentation des dépôts fluorés du système locomoteur.

(2) On présente des tableaux comparés de spondylite rhumatismale, de fluorose mutilante et de carcinome métastatique.

Comparación de la espondilitis reumatoide y de la fluorosis mutilante

SUMARIO

(1) Se determinaron las cifras de fluor en fragmentos de autopsia de costillas, sacro, iliún, vértebras, tejidos blandos adyacentes y médula costal de un sujeto con espondilitis reumatoide de 10 años de duración. Las cifras de fluor no rebasaron las normales. En este caso la condensación ósea que se suele encontrar en esta enfermedad no fué debida al aumento de los depósitos de fluor en los tejidos del sistema locomotor.

(2) Se presenta una comparación tabulada de la espondilitis reumatoide, de la fluorosis mutilante y del carcinoma metastásico.