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Hyperparathyroidism causing osteitis fibrosa cystica versus fibrous dysplasia of bone

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HYPERPARATHYROIDISM
CAUSING OSTEITIS FIBROSIA CYSTICA
VERSUS
FIBROUS DYSPLASIA OF BONE

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Introduction and History

Since von Recklinghausen described, in 1891, (1) a bone condition called osteitis fibrosa cystica, much confusion has resulted in the exact interpretation of the term. The name came to include a variety of bone dyscrasies.

Generalized osteitis fibrosa cystica, due to hyperparathyroidism, is exemplified in von Recklinghausen's description of cases #5 and #7 (Hunter 2) which disease entity bears his name. These cases would probably have shown an adenoma of the parathyroid glands, had a search of that region been made.

The relationship between von Recklinghausen's disease of bone and malfunction of the parathyroid glands was not suspected until Erheim, in 1903, (3) wrote on the possibility of some connection between the two conditions. The etiology was finally established in 1925 by Mandl (4) when he cured a patient by the first parathyroidectomy.

The medical profession is just beginning to recognize the frequency of hyperparathyroidism, especially the subclinical cases.

However, some surgeons have been overly enthusiastic cutting the throat of those people who have bony deformities due to osseous dysplasias, thought to be due to a possible adenoma of the parathyroids. In numerous cases, no tumor was found, and many times futile second exploratory operations were done. Fibrous dysplasia of

bone is one of the cystic lesions of bone which is frequently misdiagnosed and too often treated as hyperparathyroidism.

The clinical condition of osteitis fibrosa cystica was described as early as 1877 by Langendorff and Mommsen (5), but they failed to differentiate it from other forms of osteomalacia. Herschberg, in 1889, (6), described this condition as leading to osteomalacia. In 1891, von Recklinghausen (1) actually separated and named "osteitis fibrosa cystica" as distinctive from other bone dyscrasias.

Von Recklinghau(1) describes Case 5 as a broadening, deforming osteitis with tumors and cysts oc-curring in a 66 year old woman, who died of pneumonia. The postmortem findings were given. There was marked deformity of the lower extremities with outward bowing of the limbs. The skull was grossly thickened. Both femora and the right humerus were deformed. The upper ribs were distorted and porous. The bone marrow in these areas showed eburnated bony areas, large islands of fibrocartilage, spongiosa, marrow tissue and large cysts, the largest being 5cm in diameter. In discussing Case 5, von Recklinghausen emphasizes that the lesions described by Paget do not show cystic formation. He viewed osteitis fibrosa cystica as an end stage of osteomalacia.

When Mandl (4) performed the first parathyroidectomy in 1925, the relationship between osteitis fibrosa cystica and the parathyroids was established. Looking backward, we find that Sandstrom in 1880 (7) was the first to describe the parathyroid glands. Welsh in 1897 (8) gave a very fine description of the parathyroid glands. Since the first parathyroidectomy, much has been written on surgery of the parathyroid glands, their variations in position and blood supply. A discussion of the anterior of the parathyroids will not be attempted.

Etiology

Primary osteitis fibrosa cystica results from an adenoma of the parathyroid glands. In 1937 Gilmore and Martin (8) reported that in women there is a progressive increase in the weight of the parathyroid glands up to 50 years of age, whereas in men, the maximum weight of the glands were reached between 21 and 30 years of age, possibly accounting for the higher incidence of adenoma in women. The cause of the adenomata is obscure. The resulting condition is called primary hyperparathyroidism.

Secondary hyperparathyroidism may result as a compensatory mechanism from the chronic loss of calcium due to a chronic glomerulonephritis.

The primary and secondary hyperplasia are difficult to differentiate except histologically. If there is a

long history of kidney trouble, secondary hyperplasia is the most likely condition.

Not until 1937 did Albright (9) and his associates describe a trio of conditions which became known as "Albright's syndrome". The osseous component was a fibrous dysplasia of bone. Other names applied are osteodystrophia fibrosa unilateralis and polyostotic fibrosis dysplasia, localized osteitis fibrosa cystica, osteitis fibrosa disseminata, osteitis deformans juvenilis, juvenile Paget's disease and atypical neurofibromatosis.

The triad described by Albright included:

(1) Multiple bone cysts, with a distribution suggesting a relationship to nerve roots or to an embryonic defect in the myotomes.

(2) Areas of pigmentation which have a distribution suggesting some connection with bone cysts.

(3) Precocious puberty in females but apparently not in males.

The great majority of fibrous dysplasia are unassociated with changes in pigmentation or precocious puberty.

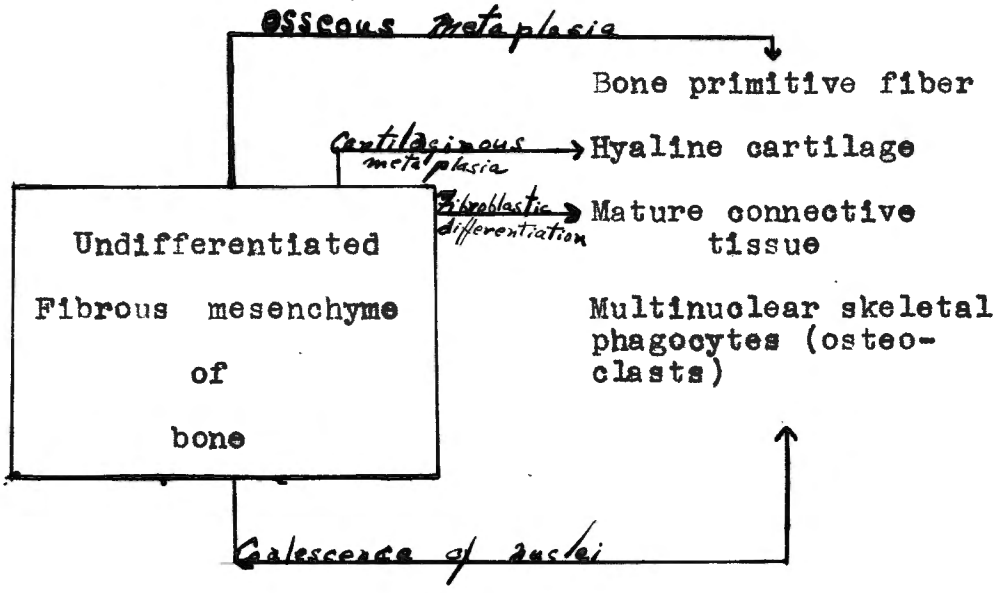
The bone cysts were often confused with osteitis fibrosa cystica and operated on for a tumor of the parathyroids.

The etiology of fibrous dysplasia of bone is uncer-

tain. Albright (9) suggested that since precocious puberty was not present in the males that the syndrome is due to a disturbance in the follicle stimulating hormone of the anterior pituitary.

Falconer and Cope (10) remark that four cases of fibrous dysplasia of bone have been recorded who had been followed because of icterus gravis neonatorum. They suggest that there may have been some nuclear involvement of the brain. They also suggest that the focal distribution may be explained on a hormonal basis, a pituitary disfunction with an increase in the production of gonadotrophic, thyrotrophic, and growth hormones. They have never found a case in which there were ovarian or adrenal tumors. They also record 2 cases in which the appearance of the symptoms were directly referable to anterior poliomyelitis. Neller (11) also mentions the high incidence of severe jaundice or gastrointestinal disburbances in the neonatal period and suggests an enlarged thymus may be the causative factor. He goes on to say that it seems improbable that any single fact can account for all elements of the syndrome. Lichtenstein (12) said that the condition of fibrous dysplasia of bone may represent merely a "misdirected metamorphosis of the mesenchymal stem cells of the bone". This is the most likely explanation for fibrous dysplasia of bone.

Chart from Lichtenstein:



Lichtenstein goes on to state that myxomatoid tissue probably results from hydroptic degeneration in areas of poor blood supply.

Goldhamer (13) thinks that the precocious puberty might result from involvement of the base of the skull producing pressure on the hypothalamic region.

Sternberg and Joseph (14) state that complete sympathectomy has no effect on growth and development of bone. From this the reader is lead to the conclusion that the etiology of osseous changes is not on a sympathetic basis.

Relative Incidence:

The incidence of osteitis fibrosa is more common than the ordinary practitioner suspects. The classical form is rare and offers no diagnostic difficulties. As

Albright and his associates state (15) "hyperparathyroidism is a common and polymorphic condition ... and the diagnosis must be considered and ruled in or out when any of a whole list of presenting symptoms of the most varied nature is encountered".

Wilder and Howell (16) in 1936 showed in graphic form that from all statistics that they could gather the incidence of hyperparathyroidism in the North Atlantic states was greatest; Scandinavia, Belgium and Holland next; England and Scotland; upper Mississippi Valley followed by Germany and Austria; France and Italy last in incidence.

They suggested that this might be related to the lack of ultraviolet radiation (Vitamin D). But the ricket belt and the hyperparathyrodism belt do not coincide.

Jaffe said (17) that there was no sex difference, but most authors are agreed that the ratio of females to males is about 3 to 1. The age incidence varies considerably, but the majority of cases occur between 30 to 50 years of age.

Predisposing causes may be a renal insufficiency. Heredity, however, does not seem to enter the picture. Cases of fibrous dysplasia of bone also seem to be more prominent in the females. Gorham (18) and Lichten-

stein (12) give a ratio of 3 females to 1 male. There is no hereditary tendency. The age of awareness seems to be between 1 and 20 years. Sufficient cases have not accumulated for accurate figures on the geographical and racial occurrence of fibrous dysplasia.

Signs and Symptomatalogy of Hyperparathyroidism

The symptomatalogy of hyperparathyroidism can be divided into 3 groups:

(1) that caused from hypercalcemia or general symptoms.

(2) that related to skeletal manifestations.

(3) that related to renal conditions caused by an increased excretion of calcium and phosphorous in the urine.

General Symtoms

Just as hypocalcemia causes an increased excitability of the nerve - muscle apparatus so hypercalcemia causes the opposite signs. There are numerous symptoms (Helfet-19) including hypotonia, lassitude, anorexia, weakness, and general physical and mental indifference. The gastrointestinal symptoms include abdominal pain, especially in the younger individuals (Jaffe - 17), and constipation, often whitish hard stools. There may be a coldness and bluish discoloration of the extremities, and a sallow com-

plexion. Helfet (19) reported a few cases with brown pigmentation. These may have been cases of Albright's syndrome. Helfet also observed cases with a mild dry eruption on the face. Albright, Aub, and Bauer (15) state that there is often flat feet due to a hypotonia. They also mention that there is a weight loss probably due to the anorexia. Associated with this, the individual may have an anemia with a leukopenia. (Boyd - 20). Shelling (21) found that in many cases there is a bradycardia. In the functional type of Leopold (22) there was insomnia. Gorham (18) states that there are often disturbances in gait.

Skeletal Manifestations

Symptoms related to the skeletal manifestations include early diffuse tenderness, aches and pains, many times loosening of the teeth, and jaw pain are the first signs says Helfet (19). He also states that arthritis is frequently responsible for the first signs of parathyroid disease. Often there is dull lower backache and in the arms and legs there is pain which is intensified by exercise, and many times associated with stiffness of the joints. Late in the disease, bony deformities begin to take place. Often the first noticeable signs of bone change are in the vertebral column. There is a shortening of the stature, due to kyphosis and scoliosis. Be-

cause of the vertebral changes there may be a deformity of the thoracic cage. Bowing of the femoral shafts may be present. The pelvis may be distorted. The skull may be thin, atrophic and pliable, or it may be thickened. A spontaneous fracture is often the first event which brings the patient to the doctor. Albright et al (15) described a case which died because of total loss of use in inability to raise the thorax in respiration.

Renal Symptoms

Symptoms related to renal conditions caused by an increased excretion of calcium and phosphorus in the urine include; first, renal colic which Wilder and Howell (16) said preceded the evidence of disturbed calcium metabolism in 18 or 135 cases (13.3%). Adams (23) said that he had looked for disturbed calcium metabolism in many patients with renal colic, but as yet has not discovered any with a change in the blood chemistry. There is often polyuria and polydypsia nocturia, and enuresis, urinary gravel, or"sand". Helfet (19) said that prolonged hyperthyroidism constantly results in renal failure usually accompanied by calcification of the kidneys. The calyces may be outlined well in a radiograph.

Signs and Symptomatology of Fibrous Dysplasia

Fibrous dysplasia of bone offers fewer symptoms

than does osteitis fibrosis cystica. Fibrous dysplasia is exhibited by: (1) physical changes in the body from bony deformities with occasional endocrine or pigmentary changes. (2) There may be bone pain, but this is not marked. In a majority of Albright's cases, females, 70% (11), menarche often occurs within the first few years of life, average age being 3 years, Neller (11), and has even been recorded at a few months of age.

Neller (11) states that in many, there are additional elements such as a notable number of goiter individuals who show signs of hyperthyroidism. Falconer and Cope (10) also state that nodular or diffuse enlargements of the thyroid have been noted more than an accidental occurrence would allow. Some were toxic. They also reported some with acromegalic features, especially unilateral (Weber - 24), coarseness of facial expression, slight prognathism, and enlargement of the tongue, hands and feet. In some, they found gynaecomastia associated with other characteristics of the female. Albright et al (9) did not note any precocious puberty in males. The precocious puberty, they said, was unusual in that it does not lead to sterility or other endocrine disturbances. Lichtenstein and Jaffe (25) recorded 20 of 90 cases (22%) showed indubitable clinical signs of endocrine dysfunction. The majority were females, children or

young persons with a history of premature skeletal growth, and maturation.

Skeletal manifestations of fibrous dysplasia are few. There may be palpable enlargement of an extremity such as the shaft of a femur. Falconer and Cope (10) state that in absence of trauma, the progressive lesion is painless. Often there is fracture of the upper end of the femur, which is relatively painless and unites readily, usually in a coxa vera position. They go on to say that scattered foci of fibrous dysplasia remain symptom free. Lichtenstein (12) says that his cases had pain, limp, and deformity, which were of long duration. Leontiasis ossea often was a marked feature and was some-times associated with definite proptosis and visual de-terioration of the eye (apparently due to the great bony overgrowth of the base of the skull compressing the optic nerve and encroaching on the orbit). The individual may have stunted growth because of premature fusion of the epiphyses.

Diagnosis of Hyperparathyroidism

In the diagnosis of hyperparathyroidism, we have four avenues of approach;

(1) Blood and urine chemistry
(2) X-ray interpretation
(3) Biopsy

(4) History, including the patient's deformity and palpation of the tumor mass in the neck.

Chemical changes in hyperparathyroidism are;

(1) Hypercalcemia

(2) Hypercalcemuria

(3) Hypophosphatemia

(4) Hyperphosphatemuria

(5) Hyperphosphatasemia

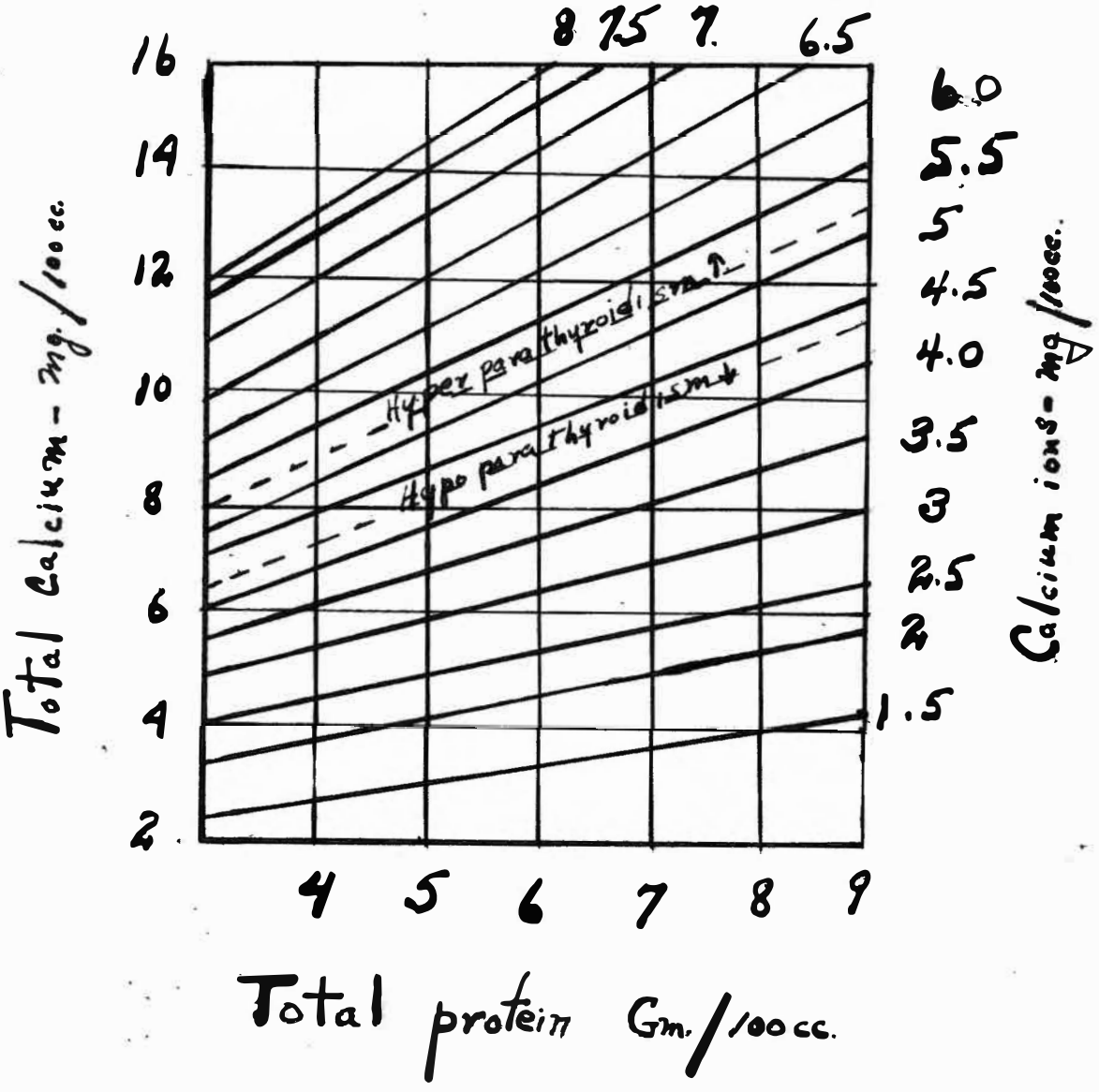
Normal blood calcium varies between 9 - 11 mg. per-cent. Hypercalcemia is said to be present when the calcium level is above 11 mg. per cent. Steward and Percival (26) made studies of calcium metabolism, and concluded that 99% of the body calcium is present in the skeletal system in the form of calcium orthophosphate and calcium carbonate in equilibrium with blood calcium, so that the latter is kept at a constant level. A generally accepted composition of a blood calcium is;

Calcium proteinate ----------5.mg.%
Calcium ions----------4.5mg.%
Non-ionized calcium citrate---- .5mg.%

Total -10.0mg.%

The parathyroid glands control the amount of ionized calcium in the blood stream (26). The calcium ions and the calcium proteinate are in chemical equilibrium, and their relationship depends on the total amount of the total serum protein. The activity of the parathyroid glands

can be judged from the amount of oaloium ions in the serum McLean (27) devised a chart to determine easily the amount of calcium ions pr0sent, from knowing the total serum cacium and the total serum protein.



Parathyroid hormone was extracted as early as 1924 by Hanson (28). The hormone was isolated by Collip (29) in 1925 and called "parathormone Collip". Albright et al (30) in 1929 described the effects of increased parathyroid hormone on the body. Once the diagnosis is suspected its confirmation or exclusion can be determined

chemica laboratory. Other diseases may give altered calcium and phosphorus levels, but no others give the combination of hypercalcemia and hypophosphotemia. However, when the disease is marked and has progressed to renal insufficiency, the serum phosphorus level may be normal or elevated. Any calcium level above 11 mg. % or any phosphorus level below 3.5 mg. % should be considered very suspicious. Technique of determination is important. Serum should be taken in a fasting state, and cleanliness is mandatory (15).

Phosphatase splits inorganic compounds to liberate organic phosphorus, to symthesize organic compounds, and to utilize organic phosphorus. The plasma phosphatase level, says Albright et al (15), probably indicates the degree of osteoblastic activity. In Bodansky's (31) method, the normal range is from 2 - 4 units. The degree of bone pathology is indicated by the level above the normal. A normal phosphatase level does not exclude hyperparathyroid -ism. Christopher (32) states that a phosphatase level is of help in diagnosis, but its principle usefulness is in

following the progress of any one case.

X-rays

Diagnosis of osteitis fibrosa cystica by x-ray is often confirmatory in nature, or the patient usually comes to the doctor because of a fracture and the condition picked up accidentally by x-ray.

All bones show a generalized demineralization, a miliary mottling, a ground glass appearance, which may be very similar to that of osteomalacia and senile atrophy.

Often a finely porous hypertrophy of the vault of the skull is present. (Hodges, Phemister, and Brunschwig (33). Pagetoid changes in the skull occur rather frequen-

tly. However the dense areas of the skull, such as are seen in Paget's Disease, are rarely present. Camp (34) and Dresser and Hamptom (35) mention that the skull was thickened from .5 - 1cm. above the average. The inner and outer tables were not distinguished, and the diploe usually not being visualized. The sella turcica is unchan-

ged except for demineralization. The middle fossa may be somewhat flattened. Cystic areas may be in the mandible and maxilla, and alveolar resorption may be present.

The vertebral bodies show, in addition to osteoporosis, a perpendicular striated fibrocystic change. Depen-ding on the extent of the disease process, the bodies may be normal or narrowed, showing compression deformities re-

sulting in kyphosis, scoliosis, and a diminution of the height of the body. A lateral x-ray of the lumbar vertebra often show biconcave discs (fishbone vertebrae), Albright et al (15).

The pelvis shows the same general characteristics, cystic formation, and alteration of contour, which suggests a richitic type or sacroiliac arthritis.

The ribs are decalcified and frequently have cysts on the superior and inferior margins.

The extremities show osteoporosis, often cystic areas near the ends of the diaphyses. There is no periosteal proliferation and no soft tissue tumors. Often there are evidences of old healed fractures. In young persons there may be a slipping of the epiphyses. Joint surfaces may collapse in small bones simulating a destructive arthritis.

A film of the lungs and abdomen may show metastatic calcium deposits in those organs in which the pH tends to be on the acid side. Therefore it is not uncommon to see renal calculi, deposits of calcium in the lungs, gastric mucosa, (Holmes and Ruggles (36). Albright et al (15) says that occasionally x-ray may show the tumor mass when in the anterior mediastinum.

Biopsy

The third means of diagnosing osteitis fibrosa cystica is by a bone biopsy. Its characteristics will be discussed in a section dealing with "Pathology".

History

The fourth manner of diagnosing hyperparathyroidism is on the long history of multiple symptoms which were discussed under "Symptomatalogy", the actual deformity of the patient's bones, and in 10% (Gutman et al (37)) of the cases by the palpation of a tumor mass in the neck. The age of the patient is often between 30 to 50 years. Often from the history alone, the diagnosis may be made.

Diagnosis of Fibrous Dysplasia

The diagnosis of fibrous dysplasia is made on;

(1) X-ray examination

(2) Biopsy

(3) Clinical History

X-ray

The x-ray examination of the bones may be confusing. Gorham (18) states that the lesions are scattered, localized, and multiple, with considerable portions of the skeleton uninvolved. There is no generalized demineralization of bone as in osteitis fibrosa cystica and osteomalacia. The appearance is more like that of Paget's Disease and xanthomatosis. Here, there is a tendency for unilateral involvement. It is emphasized that there are areas of inoreased density, representing overgrowth of hone as well as areas of decreased density. There are portions of the skeleton which have normal Bone. The epiphyses are

rarely if ever involved. Falconer and Cope (10) state that the original bony architecture is absorbed and circumscribed areas of rarefaction are visualized by x-ray. As the cancellous bone is displaced by fibrous material, the cortex becomes thin. They go on to say that the irregular dense trabeculae cross the involved area in all directions, producing an appearance suggestive of a polycystic condition. They add that no cysts are actually present. McCune and Bruch (39) described the appearance as that of "an indescribable confusion of shadows of greater and lesser density, which result in an appearance best likened to a column of slowly ascending smoke." Lichtenstein (12) states that the trabeculated appearance reflects irregularities in the extent of erosion of the inner surface of the cortical bone. Secondary deformities are usually present and fractures are not infrequently found. In order of frequency of involvement are the femur, tibia, humerus, radius, skull, jaw, pelvis, ribs and phalanges. Falconer and Cope (10) state that there is a tendency toward regional unilateral distribution. The epiphyses usually are not involved even though the entire shaft is involved, but once union has taken place, involvement may extend from the shaft. They go on to say that the bones of the base of the skull and of the face are often involved in a sclerotic overgrowth. If the face bones are

involved, it is usually unilateral and a gross asymmetry is apparent. From the sclerotic overgrowth of bone there may be pressure on the optic and olfactory nerves. The sinuses, especially the frontal, may be obliterated. The sella turcica may also he obscured. The skull may show an irregular patchy thickening of the bones, "pagetoid" in appearance. The thickening is usually marked in the frohal region and particularly the outer table of the skull.

Biopsy

The nature of the biopsied specimen will be discussed under "Pathology". From the biopsy specimen it has been claimed that a diagnosis may be made, but the picture is so varied in nature that it is difficult. A diagnosis by this method would have to be made by a skilled pathologist who has studied and interpreted a number of cases of fibrous dysplasia of bone.

History

The history of precocious puberty in girls and of early bony abnormalities and fractures is very suggestive of fibrous dysplasia of bone. Cases of fibrous dysplasia of bone do not have to have all of the triad of symptoms of the syndrome Albright (9) described. Gradations of the disease exist. The symptoms found were discussed under "Symptomatalogy".

The blood chemistry studies are usually normal, except phosphatase which is usually elevated.

Differential Diagnosis

The differential diagnosis of osteitis cystica and fibrous dysplasia of bone is usually easy, however the former mimics many diseases and vice versa. The diseases which must be considered and the outstanding differential points of each are considered in the following table which is given by Albright et al (15) on the following page.

DIFFERENTIAL POINTS REGARDING -

	SYMPTOMS		BIOPSY
1. Hyperparathyroidism bone involvement	Bone, pain deformity, fracture, tumor, hypotonia, polyuria realting to stones and disturbances	General demineralization of bones, deformity, cysts, tumors, fractures, stones	Rarefied bone; and fibre- of marrow, osteoclasts ↑ osteoid tissue only slightly increased osteoblasts ↑ ↑ ↑
2. Senila Osteoporosis	No bone tumor polyuria stones	No cysts, tumors or stones, rarified areas of bone	No fibrosis of marrow, osteoclasts normal, osteoid tissue, normal or decreased; osteoblasts decreased
3. Pagets' Disease	Bones enlarged; no polyuria; stones infrequent	Polyostotic but not generalized; bones hypertropied, eg. thick skull	May occasionally be difficult or impossible to differentiate mosaic pattern
4 Osteomalacia	No bone tumor polyuria or stones	No tumors or stones bending deformities	Ostoid tissues ↑ ↑ ↑ Ostoblasts ↑ ↑; Osteoblasts decreased
5 Solitary cysts	Confined to cysts	No generalized changes; cysts may be multiple	Cannot differentiate if taken from lesion
6 Solitary benign giant cell tumor	Confined to tumors	No generalized changes	Cannot be differentiated if taken from lesion.
7 Osteogenesis imperfecta	Fractures ↑ ↑ no bone tumor, polyuria or stones	Cysts rare; no tumors or stones	No fibrosis of marrow osteoclasts normal
8 Multiple myeloma	Can cause same bone symptoms and renal symptoms	Can almost be indistinguishable	Tumor tissue
9 Metastatic malignancy		Bones not involved, normal, seldom effects bones of forearms' or lower legs	Tumor tissue
10 Basaphilic Adenema pituitary (cushing)	Amenorrhea, obesity & hirsutism	Usually only osteoporosis	

	CALCIUM	PHOSPHORUS	PHOSPHATASE	MISCELLANEOUS
1	High	Low	High	All age groups, majority 30 to 50 years
2	Normal	Normal or low	Normal	
3	Normal or slightly high	Normal or slightly high	Very high	Age group-middle age and later seldom under; usually involves lower extremities. Runs in families. Arteriosclerosis + + +
4	Normal or low	Low	High	Practically absent in this country, except with fatty diarrhea
5	Normal	Normal	Normal	
6	Normal	Normal	Normal	
7	Normal	Normal	Normal or very slightly elevated	Hereditary, often coupled with a blue sclera and deafness; improves after cessation of growth
8	Normal or high	Normal or high	Normal	Bence-Jones proteinuria
9	Normal or high	Normal or high	?	Primary focus
10	Normal	Low	?	Abdominal striae, Hypertension

Cont'd.

The ten conditions listed in the table are to be considered, but the diagnosis may almost always be made from a hypercalcemia and a hypophospatemia. The only condition in hyperparathyroidism in which there isn't a hypophospatemia, but a hyperphosphatemia, is when there are considerable metastatic calcium deposits in the kidney and the calcium blood level is above 14 - 15 mg. %. A few words will be said about the ten conditions above and a few remarks about renal rickets and xanthomotosis.

Because of muscle weakness and fatigue one is forced to consider:

(1) Addison's Disease
(2) Neurasthenia
(3) Myasthenia gravis
(4) Progressive muscular atrophy
(5) Hypoparathyroidism
(6) Anemia

These usually are easily ruled out from a neurological and blood chemistry test.

In senile osteoporosis, the bone is qualitatively normal and only quantitatively diminished. As Albright et al (15) suggest, this condition may be produced by an underactivity of the osteoblasts or hyperactive osteoclasts, giving rise to bone pain, fractures, and deformities. This condition is quite difficult to differentiate from hyperparathyroidism, especially because of borderline blood values.

In Paget's Disease, there is often poly ostotic con-

ditions but is never generalized as in osteitis fibrosa cystica. Even with a biopsy, this condition is often very difficult to differentiate from hyperparathyroidism. X-ray and laboratory studies are usually best. Falconer and Cope (10) state that there is a loss of contrast between the cortical and trabeculated bone, with the formation of a new pattern of interlacing trabeculae, and there may be a fibrosis of the marrow spaces. The thick skull with a moth-eaten appearance and more coarse mottlings instead of a thin skull of a ground glass appearance of hyperparathyroidism helps to differentiate the two conditions.

Osteomalacia, or adult rickets, is only seen in the malnourished, multiple pregnancies and fatty diarrhea. There is a failure of calcium to be deposited in the osteoid tissue giving a widening of the osteoid seams. Other differential points are listed in the table on the differential diagnosis.

"Solitary" cysts and solitary benign giant cell tumors are easily differentiated from hyperparathyroidism by normal blood calcium, phosphorus, phosphatatase levels and usually the absence of any other skeletal involvement.

In osteogenesis imperfecta there may be multiple fractures, being generalized in nature, hereditary tendencies,

blue sclerae and deafness. A characteristic feature is the appearance of small plaques of bone in the skull united by fibrous tissue, giving a mosaic pattern. (Holmes and Ruggles (36)).

Multiple myeloma may simulate hyperparathyroidism in the x-ray, but a lack of hypophosphatemia, biopsy, and Bence - Jones proteinuria give the most aid in making a diagnosis.

In metastatic malignancy, it shouldn't be difficult to find the primary lesion. There may be a hypercalcemia but not a hypophosphatemia.

Basophilic adenoma of the pituitary gives evident endocrine disturbances. However there is an osteoporosis in association with this condition. There is evidence that a Cushing's disease may cause a hyperplasia of the parathyroid gland, which could develop into an adenoma. Schmorl (39).

Differential Diagnosis of Fibrous Dysplasia of Bone

The diseases to be considered in the differential diagnosis of fibrous dysplasia of bone are practically the same as those of hyperparathyroidism. The following diseases are also to be included for consideration.

Von Recklinghausen's neurofibromatosis must be considered, but the skin lesions are often diagnostic. Biopsy insures the diagnosis. Considerable similarity exists between these two conditions.

Ollier's disease, unilateral dyschondroplasia, gives no marrow fibrosis or fibrous replacement. There are islands of cartil ge either within the cortical bone, or else as isolated zones between the surviving trabeculae. Falconer and Cope (10). Onset in childhood is frequent.

In osseous xanthomatosis, there is a decreased density in the medullary spaces. Biopsy shows typical foam cells.

Giant cell sarcoma may be ruled out by biopsy.

Fibrous dysplasia of bone is more like Paget's Disease and xanthomatosis in appearance.

Pathology

The pathology of osteitis fibrosa cystica involves a discussion of the parathyroid changes and the osseous changes. Only a brief discussion of the parathyroid pathology will be given.

An adenoma of any of the cells of the parathyroid may be the offender. In the adenoma, primary hyperparathyroidism, there is a uniform differentiation of the cells to a large water-clear type. In secondary hyperparathyroidism, the tissue is made up of normal sized "chief cells" with a marked increase of oxyphil cells, and only a few small water-clear cells Boyd (20). The cells of the adenoma are usually large and clear, ballooned in ap-

pearance, resulting from their rich glycogen content, and are usually arranged in columns or cords. The secondary hyperplasia may result from chronic renal disease, rickets, osteomalacia, multiple myeloma, and Cushing's syndrome. Soffer and Cohn (40). Boyd (20) states that those patients with chronic renal disease that have been examined had a mean parathyroid weight 50% above normal. The hyperplasia is present in all of the glands of the parathyroid tissue as a compensatory mechanism, whereas the adenoma affects only one gland of the parathyroids. However there have been some who have advocated that there may be hyperfunction of the glands without either hyperplasia or tumor present (16).

The pathology of the osseous system will now be discussed in more detail.

As was mentioned previously, in hyperparathyroidism, there is a generalized demineralization of bone, not too unlike the condition seen in senile or disuse atrophy in that the Haversian systems are enlarged and the trabeculae of the spongy bone are thin with greatly widened intertrabecular spaces (41). Cuthbertson and Mackey (42) explain the bone pathology as a result of a generalized and a focal process going on simultaneously. In the generalized process, resulting probably

from an osseous hyperemia, the calcium phosphate com-plex goes into solution leaving an osteoid tissue which reverts to soft, fibrous connective tissu e. The focal mechanism occurs as a result of the excess numbers of osteoclasts, causing an osseous resolution. The authors state that the osteoclasts frequently form into tumor masses. Hunter and Turnbull (2) state the process simply by saying that there is laounar resorption, apposition, fibrosis of' the marrow spaoes and the formation of osteo-olastomata and cysts. Trabeoulated -woven" bone repla-ces lamellar bone. In general resorption greatly ex-oeeds apposition, however in places, apposition is prom-inent. In rickets and osteomalacia, there is no cal-cification occurring and in osteitis fibrosa oystioa we may judge if the former ar e present by whether the amount of osteoid tissue is, or is not, excessive. In measuring the depth of osteoid zones Hunter ana Turnbull (2) found that in fibrotic areas of bone the areas of apposition was frequently as rapid as in the healing of fractures, the osteoid zones being correspondingly deep. There wes no evidence of the delay in calcification in any part of the skeleton, thus distinguishing it from os-teomalaoia and rickets. In Paget's osteitis deformans resorption and apposition of" bone are more evenly balanc-ed at first and then apposition finally taking a slight margin. The process is more ohronio in Paget's Disease.

Jaffe et al (43) found that the portions of the skeleton most susceptible to decalcification in hyperparathyroidism are those areas in which bone formation is most active. There is pronounced susceptibility to the spongy bone of the metaphyses of the long tubular bones, costochondral junction, cortices of the shafts and ribs, and the bones of the skull and lower jaw. Grossly the bones may not be deformed if the process is only moderate or in the early stages. There are usually deformities in those bones which are under stress and strain. Not infrequently evidence of multiple old fractures may be present. There is no evidence of extension of the tumor masses outside the periosteum. On cutting the bone, there is an impression of soft rubbery consistency, containing areas of a "gritty" nature. The cortex is thin. In the medullary cavities, as was described by Jaffe (41), there are scattered foci of grayish white fibrous connective tissue, in which there may be felt a small amount of finely trabeculated bone. The medullary cavity is filled with cystic spaces, some of them joining one another. The cystic areas may contain gelatinous material, albuminoid, red blood cells, and sometimes cholesterol crystals and there are some brownish discolored areas as the result of old hemorrhage. The articular cartilage is usually uninvolved,

but beneath it a slight amount of fibrosis and new bone formation occurs.

Microscopically the picture of the bones in osteitis fibrosa cystica is that of greatly increased osteoclastic activity. Osteoblastic activity is nevertheless still present. Large areas of connective tissue are present, the trabeculae are markedly reduced in size. Some are of the opinion that osteoclasts unite to form giant cells. Extravasated blood may be present. Occasionally there may be areas of osteoblastic activity predominating and cement lines appear as a result. The areas are never as numerous, irregular, or thick as those of Paget's disease. The osteoid seams are not increased in size as they are in osteomalacia. Goodman (44) believes that the fibrosis occurs as a constructive organizing process after hemorrhage into the cystic spaces. As a result of ischemia to surrounding bony structures occurs and this results in further bone destruction. Microscopically there may be evidence of old pathological fractures. These heal rather rapidly and without much pain. Hunger and Turnbull (2) state that in the fibrotic areas apposition is frequently as rapid as in the haling of fractures and the osteoid zones are correspondingly deep, but neither here nor in the available parts of the skeleton that are free from fibro-

sis is there evidence of the delay in calcification. Falconer and Cope (10) state that there are commonly some survival of the original trabecular bone and a haphazard arrangement of the fibre bone trabeculae.

Lichtenstein and Jaffe (25) mention the "scalloped erosion" under the periosteum in hyperparathyroidism.

Chemopathology

The following discussion will deal with abnormal chemistry which occurs in hyperparathyroidism, and as related to the blood and osseous system.

The principal changes in the body chemistry that occur are changed blood phosphorus, calcium, phosphatase, and parathormone levels; possibly an altered pH and some lack of vitamin D.

Phosphatase, an enzyme, which splits inorganic compounds to liberate organic phosphorus, to synthesize organic compounds, and to utilize organic phosphorus. Kay in 1932 (45) found that the blood phosphatase was increased in Paget's Disease, osteomalacia, infantile rickets, adolescent rickets, renal rickets, and in generalized ost itis fibrosa cystica. Highest concentration occurs in cartilage undergoing calcification. In the body tissues, it is found chiefly in the leucocytes, intestinal mucosa, and the kidney. Kay decided that rise

of plasma phosphatates was a secondary phenomena. It represents the degree of osteoblastic response of the tissue, without regard to the bone disease. The serum phosphatase normally is 2 - 4 Bodansky units. In established cases of hyperparathyroidism the phosphatase level is elevated, but never as high as is found in Paget's disease where the level may be as high as 100 units.

Blood calcium and phosphorus levels are controlled by the parathormone output of the glands, the efficiency of the kidneys, vitamin D, and calcium excretion in the stools.

Parathormone results in an increase of the ionized blood calcium, resulting in an increased urinary calcium output and a negative calcium balance. By a negative calcium balance it is meant that more calcium is lost each day than is taken into the body. Parathormone causes a decrease in the inorganic serum phosphate, and there is also a tendency to form a negative phosphorus balance. Hunter and Turnbull (2) showed that 50 units of parathormone daily was found to have little effect on the level of the serum calcium, but it approximately doubles the excretion of calcium and phosphorus. They also found that 100 units a day raises the serum calcium to an average of 12.5 mg. %. Urinary calcium increases to six times the normal level. Parathormone cau-

ses an increase in the blood volume. It increases in the absence of vitamin D by compensatory hyperplasia of the parathyroid glands. Soffer and Cohn (40) say that the parathormone is concerned chiefly with metabolism of calcium and phosphorus, especially with the mechanism of excretion of these ions. Parathormone lowers pH toward the acid side without affecting the carbon dioxide combining power. This seems unreasonable because of the effective carbonate buffer system. Selye (48) in working with parathormone came to the conclusion that the primary point of action is on the bone and not the kidney, because complete nephrectomy on the rat does not prevent the action of the parathormone on bones. Parathyroidectomy, he found, prevents the bone changes caused by nephrectomy. Nephrectomy alone causes bone changes similar to those caused by parathormone, although they are mild and develop more slowly, possibly through stimulation of parathormone through parathyroid hyperplasia. He goes on to say that neither the liver nor the thyroid appears to influence the action of the parathormone.

There is a school which believes that the parathormone has its primary effect on the phosphorus metabolism, controlling the level so that it will not rise to a degree which upsets any metabolic process in which phos-

phates are concerned. Helfet (19) also believes that an accumulation of phosphate in the blood is a stimulus to the parathyroid gland with a resulting hyperplasia and increased production of parathormone. The author goes on to state that parathormone exerts its effect by stimulating excretion of phosphate by the kidney and by mobilizing calcium ions from the bones, forming calcium phosphate in the blood, and is kept in solution by the hormone. In this state it may be excreted. Helfet makes the statement that parathormone mobilizes the calcium carbonate rather than the calcium phosphate fraction of the bone salts.

Albright et al (30) found that parathormone administration gradually increases the urinary calcium excretion, without affecting the calcium excretion. Jaffe (17) stated that in the normal individual 70 to 90% of the total calcium excreted is eliminated in the stool, and the remaining 10 to 30% is excreted in the urine. He says that in hyperparathyroidism this relationship is reversed. Cessation of parathormone administration causes a gradual fall in calcium excretion below normal. When par thormone is given in conjunction with ammonium chloride the effect is more than the sum total of their individual effects - a synergistic effect occurs. The calcium level of the blood is markedly, but gradually

increased by parathormone injections, varying individually, and is more marked when the patient is on a high calcium diet. The hormone abruptly increases the urinary phosphorus excretion without affecting fecal excretion. Upon cessation of the hormone the urinary phosphorus excretion rapidly falls to a level below the normal. These changes are more rapid than those of calcium metabolism, and greater than can be explained by a theoretical calculation of the phosphorus liberated with calcium and nitrogen. Albright et al also go on to state that the phosphate level of the blood is primarily lowered by parathormone. With a rise of serum calcium above a critical level of 14 - 15 Mg. %, urinary phosphage excretion falls and blood phosphorus rises. This is probably related to a chronic high blood calcium with metastatic renal calcification. Because of the rapid alteration of phosphate levels both in the blood and the urine Albright et al (30) concluded the primary effect of parathormone was on the phosphorus, probably the excreted phosphorus being partly derived from the body tissues. They suggest a tolerance to parathormone is developed as evidenced by a decreased phosphorus excretion. They found that nitrogen excretion was not affected by parathormone. They stated that two ossifying hematomas had not been resolved by parathormone.

In an excellent article by Ingalls, Donaldson, and Albright (46), beautifully illustrated with pictures, x-rays, and microphotographs, they conclude that the effect of the parathormone on bone tissue cannot be attributed to the acidity of the hormone. In sixty hours parathormone was found to produce bone lesions, which were the same whether or not the rats were first nephrectomized, however, nephrectomy along produced bone resorption in sixty hours which were distinguishable from the lesions produced by the parathyroid extract. Nephrectomy exerted its effect on the bone by acidosis which is a slower process than the direct action of the parathyroid extract. The authors stated that the lesions produced in nephrectomized rats by parathyroid extract were present in 20 hours.

Chart number 1 was given as a means of determining calcium ion concentration of the blood in determining the activity of the parathyroids. Normally, the relationship of calcium and phosphorus may be given as:

$$\frac{[Ca^{++}]^3 \times [PO_4^{\equiv}]^2 \text{ (in the blood)}}{[Ca^{++}]^3 \times [PO_4^{\equiv}]^2 \text{ (in the urine)}} = K \text{ (a constant)}$$

If one changes, a change in the others must result. Soffer and Cohn (40) suggest that the solubility of calcium phosphage is made possible by and also limited by the pH

of the solvent medium, the CO_2 tension, the protein concentration, and the total electrolytic concentration of the medium.

Helfet (19) states that the average adult body contains 1 kilogram of calcium, of which 98% is in the skeleton. In hyperparathyroidism a loss of 150 mgms. per day for five years would amount to 28% of the total skeletal calcium. Determination of a negative calcium balance is a rather difficult and technical procedure, but is of considerable value in the diagnosis and prognosis of any case.

Pathology of Fibrous Dysplasia of Bone

The deformity of bones with fibrous dysplasia may be almost as severe as is reached in osteitis fibrosa cystica. The bony deformities often begin in infancy and progress with increase of weight until puberty or the fusion of the epiphyses. During this period of bony growth there are often multiple fractures which heal rather rapidly without much pain, leaving usually a deformity. Folconer and Cope (10) state that the process is self limiting, probably resulting from the early closure of the epiphyses because of precocity. Because of the low mortality and relatively good prognosis in these cases there have been few autopsies. Either the mem-

branous or the cartilaginous bones may be involved. The lesions in the long bones begin as multiple foci in the diaphysis, probably of congenitally malformed pre-osseous tissue or tissue without the potentialities of developing into bone. The lesions never begin in the epiphysis, and only on closure of the epiphysis does this portion ever become involved. The disease being self limited by the closure rarely extends into the epiphyseal region. Falconer and Cope go on to state that the original bony architecture is absorbed and circumscribed areas of rarefaction become visable by x-ray. As metaplasia of osteogenic tissue proceeds fibre bone is irregularly deposited and a gradually expanding lesion develops. The cortex of the bone becomes thinned, probably from pressure necrosis or ischemia. The entire bone may expand. Pathological fracture usually results, the most common site being the upper end of the femur, causing a coxa vara deformity. The authors go on to state that in the majority of the accounts of fibrous dysplasia and osteitis fibrosa cystica there is confusion as to whether the conditions are histologically identical. They say that in the majority of the reports the trabecular pattern was normal, but a fibrosis of the marrow spaces, suggesting the primary change is the fibro-

sis with secondary absorption of the laminated trabeculae and then a new formation of fibre bone. The authors say that this condition is somewhat s milar to myelosclerosis, however in the latter condition the mesenchymal cells show a hemopoietic as well as fibrillo-osteoid properties. Falconer and Cope say that with a "primary collagenous osteogenesis of the marrow with attritive osteolysis of the lamellar trabeculae", the absence of osteoclastic foci is to be expected. "A well organized fibre bone pattern" they state "is more important than the relative paucity of osteoclasts", in the diagnosis by biopsy.

Lichtenstein and Jaffe (25) say that there is little evidence of osteoclastic resorption of bony trabeculae. They describe the microscopic picture of bone as containing "immature small, slender, spindle cells in rather loose and whorled arrangement". Some areas are cellular; some areas are collagenous. In the more vital areas are located a better supply of blood vessels. They go on to state that whatever reconstruction takes place occurs slowly. The trabeculae of fiber bone are of variable size and scattered throughout the bone without pattern, seeming to be determined by blood supply.

Some more of the varied picture which may be seen is that of thin walled, engorged blood vessels, with extravasations in some areas. Multinuclear skeletal phagocytes (giant cells) may be present, smaller than

the giant cells of a giant cell tumor. Lichtenstein and Jaffe (25) say that these cells are formed from "coalescence and transformation of the stromal connective tissue cells". They make note of the fact that islands of hyaline cartilage tend to become calcified on the outside and finally undergo some endochondral ossification. The authors state that this process is closely related to skeletal encodhondromatosis. As was mentioned before, stress was placed (25) on the fact that no appreciable resorption of the outer cortex, and no scalloping erosion beneath the periosteum, was present.

The question of the presence of cysts was debatable, but now most of the workers have come to agree that cysts may be present. Falconer and Cope (10) state that the trabeculae give the appearance of cyst formation, but could find no cysts present. Sternberg and Joseph (14) say that the cysts are probably formed by ischemia, hemorrhage with bony resorption, and finally liquefaction necrosis. Lichtenstein and Jaffe (25) discovered cysts containing fluid. Their theory of cyst formation was that they could develop from: (1) hemorrhage, (2) collagenization causing ischemia, or (3) x-ray treatment.

Lichtenstein (12) says that some of the trabeculae show Howship's lacunas containing osteoclasts, without

evidence of resorption. However Sternberg and Joseph (14) state that the afflicted individuals have a "severe degree of bony destruction by osteoclastic lucunar resorption, with a heroic but inadequate attempt at repair". Gorham (18) did not find osteoclasts. Albright et al (9) say that there is a marked similarity between the biopsies of fibrous dysplasia and osteitis fibrosa cystica several weeks after a parathyroidectomy - considerable osteoblasts and fibrosis. These authors found a variety of lesions rather than any specific lesion. Because of its diffuse nature rather than generalized as in osteitis fibrosa cystica Albright et al (9) preferred to call this disease process "osteitis fibrosa disseminata". This patchy distribution is in contrast to the general demineralization of hyperparathyroidism.

An osteoblastic reaction has often been noted in the base of the skull. Leontiasis ossea is present with involvement of the bones of the face. Sternberg and Joseph (14) call the condition "unilateral acromegaly".

Falconer and Cope (10) state that the cutaneous pigmentation appears after the other symptoms. Melanin is present in the basal cells of the epidermis. They point out the similarity between the pigmentation of

that found in Albright's syndrome and von Recklinghausen's neurofibromatosis, suggesting the incrimination of the nervous system.

Abnormalities in the blood chemistry of calcium and phosphorus may occur rarely, but, as Gorham (18) says, are only changed secondarily resulting in a slight increase in calcium and a drop in phosphorus. The phosphatase level may be elevated.

There is no information available as to the cause of an early menarche.

Treatment and Prognosis

Treatment of fibrous dysplasia and osteitis fibrosa cystica may be discussed under three headings: (1) Surgical treatment, (2)X-ray treatment, (3) Medical treatment.

Osteitis Fibrosa Cystica

In osteitis fibrosa cystica the cause is an adenoma in the parathyroids. The best and safest treatment is surgical excision of the tumor mass. This may involve surgical difficulties due to abnormal position of the parathyroid tissue. Tetany may be a postoperative complication, which may be alleviated by parathormone injections, intravenous calcium gluconate, high calcium diet, and high dosages of vitamin D. Depending upon the extent of osseous damage and the amount of cal-

cium which has been lost, we may make a good prognosis with this form of treatment.

X-ray treatment has been used both locally to the bony lesions and to the parathyroid region. Merrit and McPeak (47) reported improvement or cure in six cases. Albright et al (15) got no beneficial results from x-ray therapy to the parathyroid region and advised against treatment of cystic areas because of increased fibrosis, possibly leading to an anemia. The general opinion is that x-ray treatment of hyperparathyroidism should not be undertaken unless surgical removal is impossible. In secondary osteitis fibrosa cystica, secondary hyperplasia of the parathyroids, x-ray may be very useful.

Medical treatment consists of keeping the patient in the best possible health, walking irons to avoid fractures, and a high calcium diet. This helps in preventing decalcification but also promotes renal damage. The status of vitamin D in treatment is debatable.

Prognosis of unoperated cases is poor. They become bedridden, and eventually develop renal damage sufficient to cause death. Operated cases have almost immediate recovery from pain, lassitude, and hypotonia, and the bone lesions tend to ossify gradually over a period of years. If the process has not advanced too

far before operation the bones will eventually be restored to normal.

Helfet (19) describes a method of medical treatment by prescribing aluminum acetate to combine with the phosphate in order to keep the diet at as low a phosphorus level as possible. This is not the desirable form of treatment in primary hyperparathyroidism, but the author claims remarkable results in osteitis fibrosa cystica of the secondary type. Also he makes clinical improvement in Paget's disease, rheumatoid arthritis, and in a case which seems to be a case of Albright's disease. This has not been confirmed, however.

Fibrous Dysplasia of Bone

If fibrous dysplasia is a congenital misdirected metamorphosis of the mesenchymal stem cells of bone, there is little treatment that could be considered of value. Lichtenstein (12) doesn't believe curettage and graft does any good, because the fibrous tissue fills in again. He says that pain may be aggravated by surgery, but may be advisable in fractures, and correction of bad deformities. Lichtenstein says that small doses of x-ray may be beneficial, but larger dosages may cause necrosis or a thinned cortex resulting in a pathological fracture. Sternberg and Joseph (14) state that sympathectomy has no

effect on the bone growth and development of bone. Albright et al (9) also state that x-ray may be of value locally and in small amounts.

To date no therapeutic measures have been of any real value.

Being a self limited disease, lesions of fibrous dysplasia cease their active metaplasia at adulthood. The lesions still remain without progression or repair processes occurring throughout life.

Summary

This paper has pointed out the essential differences between osteitis fibrosa cystica and fibrous dysplasia of bone. A differential diagnosis between the two conditions is primarily of importance in relation to the subsequent treatment. After the diagnosis of osteitis fibrosa cystica is established, parathyroidectomy is the specific form of treatment. Parathyroidectomy should not be done in cases of fibrous dysplasia of bone. Small doses of x-ray to the lesions of fibrous dysplasia may be of some value; beyond this, treatment is symptomatic and prophylactic toward prevention of fracture.

The following gives the basic distinguishing features of the two disease processes:

OSTEITIS FIBROSIA CYSTICA	FIBROUS DYSPLASIA
1. General Symptoms: Lassitude, weakness, GI upsets, constipation	1. No General Symptoms: May be unilateral pigmentation
2. Osseous System: Limp, bony deformity, bone pain, often fracture	2. Osseous System: Limp, deformity, often fracture, seldom pain.
3. Renal Symptoms: Polyuria, polydipsia, renal colic	3. No Renal Symptoms
4. Blood Chemistry: Calcium elevated Phosphorus decreased Phosphatase elevated	4. Blood Chemistry: Calcium normal Phorphorus normal Phosphatase may be elevated
5. Urine Chemistry: Calcium excretion increased Phosphorus excretion increased Negative calcium balance	5. Urinary Chemistry Normal:
6. History: Onset between 30-50 yrs	6. History: Onset from infancy to adulthood Precorious puberty-early menarche
7. X-Ray: Bones show generalized demineralization, cystic areas	7. X-Ray: Often lesions tend to be localized, regional and unilateral
8. Histological: Fibrous material with osteoclasts and osteoblasts, the former predominating	8. Histological: Fibrous material with few osteoclasts

FIBROUS DYSPLASIA OF BONE

and

OSTEITIS FIBROSA CYSTICA

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Case Histories

and

Photographs

FIBROUS DYSPLASIA

Case No. 1.

Mrs. N. J. Age 31.

Clinical Summary: Patient fractured left femur at three years, and has had pain in left leg all her life. Pain worse during pregnancy and menstruation. First and second pregnancies full term, (Nov. 1921, Nov. 1922). Pain worse during second pregnancy. Following this pains increased in severity with occasional pain in left tibia. Entered hospital Sept. 8, 1924 and had spontaneous fracture two days later. Very slow to heal. Symptoms less during 1929-1930. Third pregnancy in 1931 with pain beginning a few weeks after last menstrual period, but pain less severe than formerly. Ceasarian section performed on 1-14-32 with bilateral salpingotomy. No limitation of movement of extremities. Pain in abdomen on pressure.

Laboratory: 1-8-32. Hbg. 84%. RBC 4,810,000. WBC. 6,200. Blood calcium 11 mg.%. Phos. 5.5 mg.%.

X-ray: 1926. (1) Pathological fracture left femur. (2) Expanding, rarifying lesion of femur with absence of subcortical trabeculae.

1932. (3) Fracture healed. (4) Trabeculae show irregularity of width and direction with granular consistency through upper femur. Similar lesions in left pubis with expansion of cortex.

1937. (5) No essential change, indicating non-progressing lesion, probably congenital inclusion of myxomatous material.

4-26-43. (6). Pelvis, left thigh, left leg show no extension of the disease in past 17 years. Fluoroscopy of body showed no involvement in other regions.

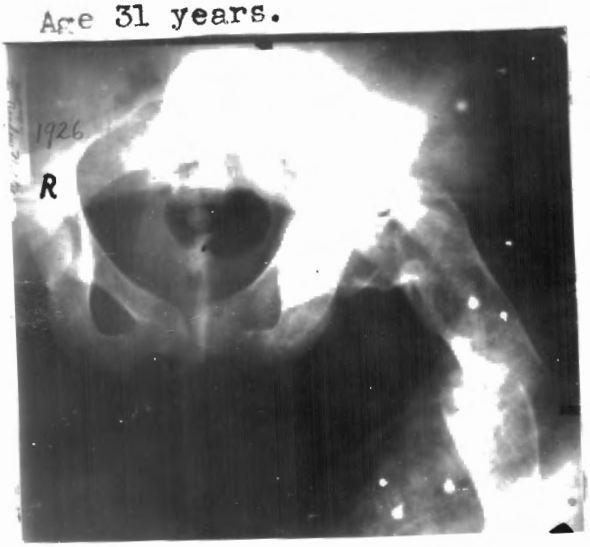
Follow-up: Patient in good general health, 4-26-43.

No hereditary transmission in three children, aged 21, 18 and 11 years.

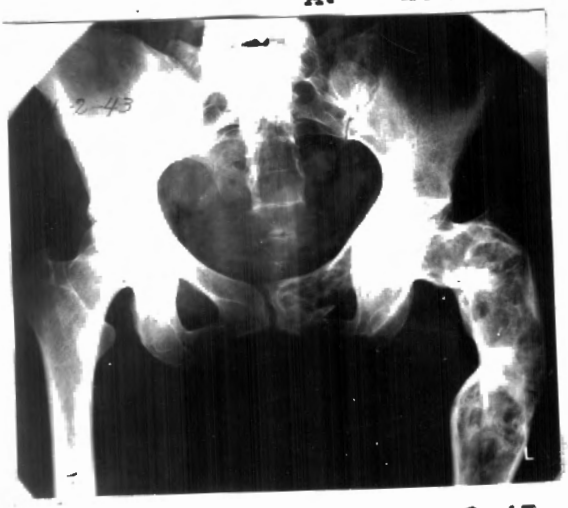
FIBROUS DYSPLASIA

Case No. 1

Mrs. N. J. Age 31 years.



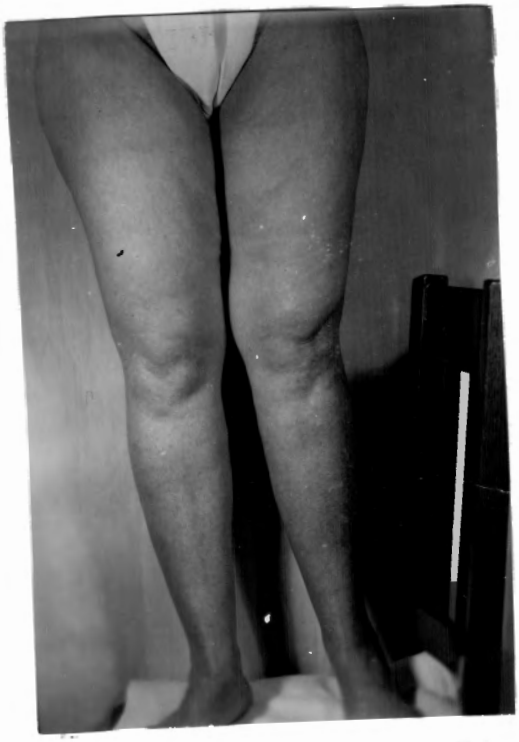
A. 1926.



B-1. 4-2-43

B-2. L. femur

B-3. L. leg



4-2-43

FIBROUS DYSPLASIA

Case No. 2.

D.M. Age 7.
First seen at age of 7 years, (1928). Exploratory operation right hip--possible diagnosis of osteitis fibrosa cystica. Fracture of upper end of femur in 1932. Pain, deformity, and loss of function right leg following trauma 12-8-34. Large fusiform swelling of right hip, very painful on movement. Shortening of right leg, lateral bowing of leg, medial bowing of ankle.

X-ray: (1) Pathological fracture of upper right femur. (2) External bowing of right femoral neck. (3) Widening of shaft. (4) Cystic areas right femur, ilium, ischium and tibia. (5) Thinning of bony cortex. (6) General granular appearance of involved bones, remaining bones normal by X-ray.

Follow-up: Biopsy right femur 12-20-34. Medullary canal--tissue with cells of uniform size, bipolar in shape. Nuclei separated by large amount ground substance and containing much fine fibrillar material. Many small well formed blood vessels. No mitotic figures; bone tissue necrotic; muscle tissue shows extensive invasion of similar tissue together with edema and degeneration.
Diagnosis: Myxosarcoma.

In this case of fibrous dysplasia with pathological fracture the appearance of neoplasm is in reality due to regeneration of bone at fracture site.

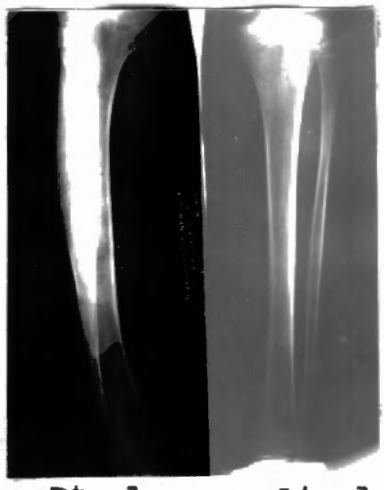
8-10-44: Patient feels fine, no pain. Now 24 years old.

FIBROUS DYSPLASIA

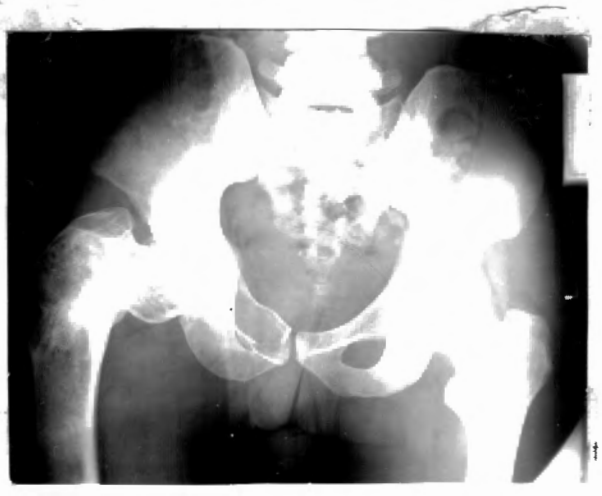
Case No. 2

D. M. Age 7 years.

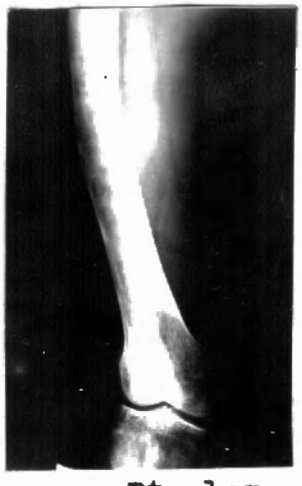
A-1. 6-7-35



Rt. leg Lt. leg
A-2. 6-7-35.



B-1. 7-8-43



Rt. leg.
B-2. 7-8-43

FIBROUS DYSPLASIA

Case No. 3.

Mrs. E. S. Age 31.

Clinical Summary: (1) Bumps on right side of head since 9 years of age. (2) Irritable and nervous since 14 years, (frequent intervals of feeling groggy and sleepy). Menarch 13 years; miscarried twice. (3) Severe headaches at intervals since 1928, more severe recently, (3-3-43).

X-ray: (1) Expanding irregular, osteolytic deposit, 3 by 4 cm. in roof of right inferior frontal region between inner and outer tables. (2) Similar expanding irregular granular deposit in right superior frontal region, 3 by 1½ cms., elevating outer table. (3) Roof of right orbit and right sphenoidal ridge are expanded and demineralized by a combined osteolytic and irregularly calcareous deposit. (4) Right anterior clinoid grossly expanded and likewise infiltrated.

Laboratory: Calcium 8.8 mg. %. P.-1.9 mg. %. Phosphatase 2.1 units, & 3.7 units.

Surgery: Operated 3-10-44.(1) Small cavity containing anthochromic fluid in right sphenoid bone tissue which eroded sphenoid ridge and orbital plate, impinging on the right optic nerve removed. (2). Mucosa of frontal sinus exposed.

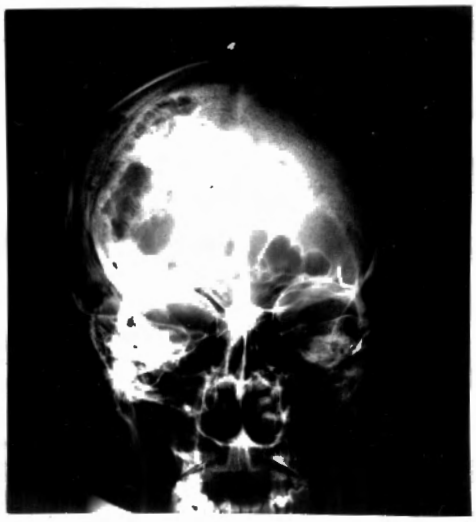
Histology report: Fibrous dysplasia of bone, probably resulting from a congenital maldifferentiation of preosseous tissue.

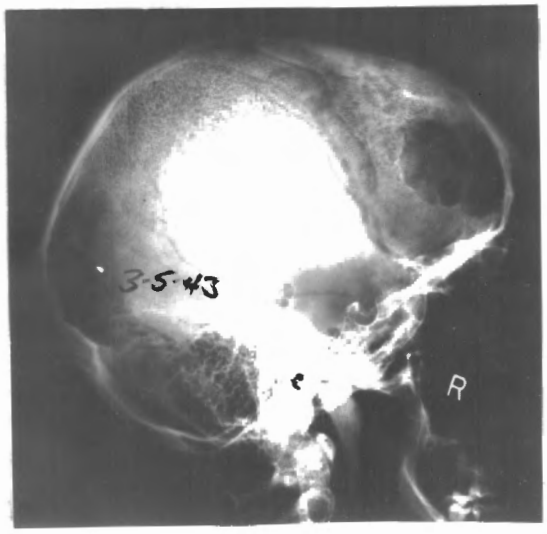
Varying histological appearance. Dense fibrous tissue with abundant matrix and numerous small hyperchromatic spindle-shaped nuclei. Another very cellular stroma marking off irregular areas of osteoid tissue. Cellular stroma is composed of spindle-shaped cells with oval hyperchromic nuclei lying in the fibrous matrix. Many giant cells--foreign body type--no evidence of malignancy.

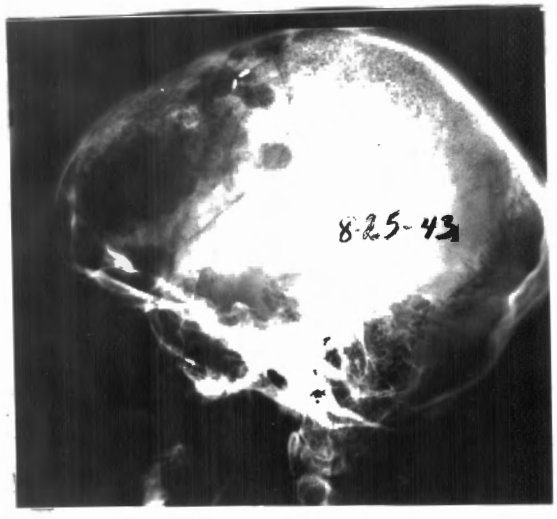
FIBROUS DYSPLASIA

Case No. 3

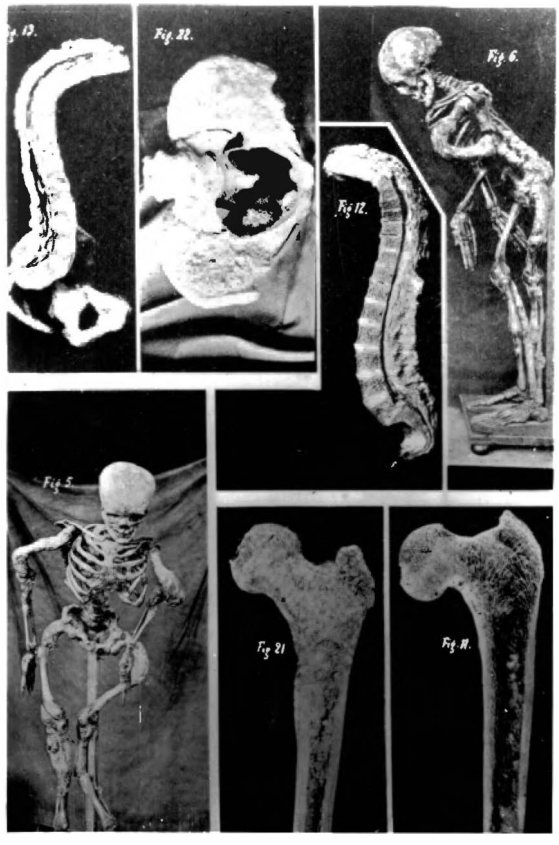
Mrs. E. S. Age 31.







OSTEITIS FIBROSA CYSTICA

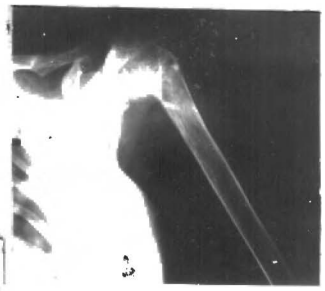


This composite photograph, from von Recklinghausen's (1) description of postmortem cases, shows grossly the generalized character of the disease process. Demineralization combined with weight bearing causes the obvious deformities.

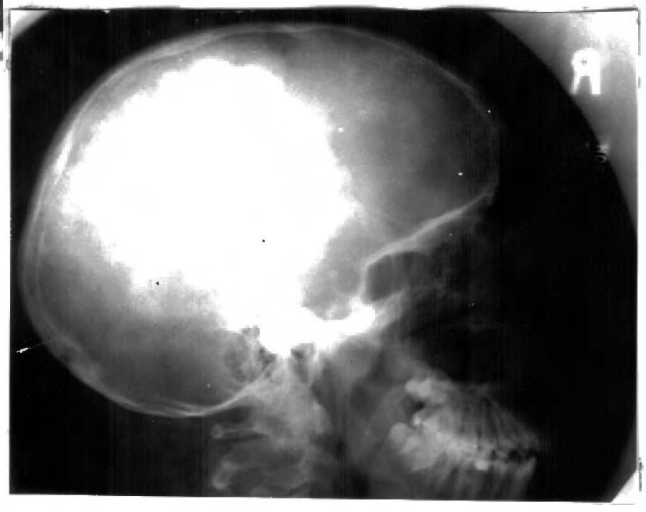
OSTEITIS FIBROSA CYSTICA

Case No. 1.

A.



B.



C.

C. B. Age 11. (1926)

Clinical Summary: Gradual bowing-in of the knee with no accompanying pain. Slipped, twisting hip, with immediate pain.

X-ray: (1) General demineralization of bony skeleton, widening of Haversian canals, thinning of cortex and trabeculae. (2) Localized complete loss of bone structure surrounded by cortex right upper and lower fibula, epicondylar regions of femora, right intertrochanteric region, surgical neck left humerus. (3) Skull showed translucent fine granular haziness and demineralization of both tables. (4) Fracture right upper femur through osteolytic area.

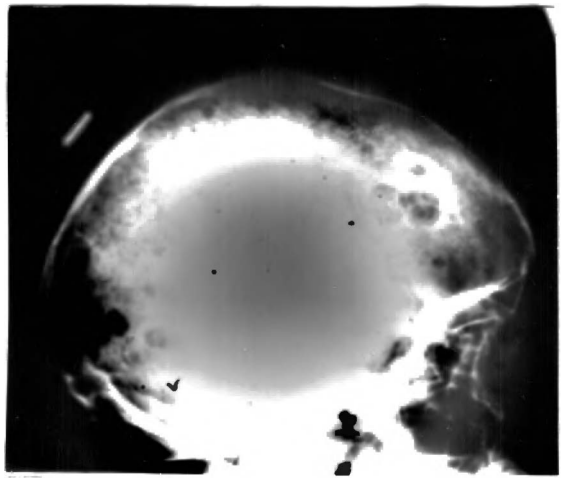
Follow-up: (1) Patient had two courses of deep X-ray treatment over parathyroid region January 1930 and April 1930.

Blood calcium 16 mg.%.

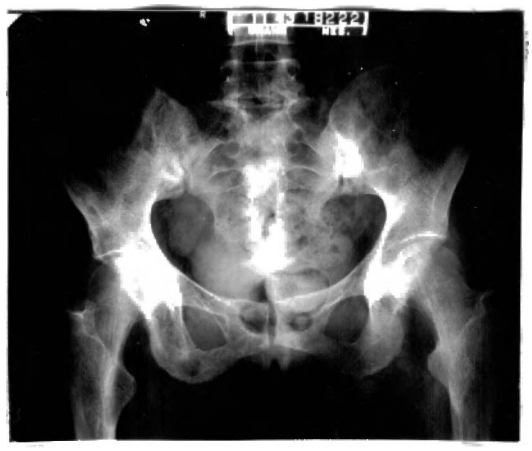
Last seen April 1932--patient up and about, wearing a molded plaster splint to prevent recurrence of fracture.

OSTEITIS FIBROSA CYSTICA

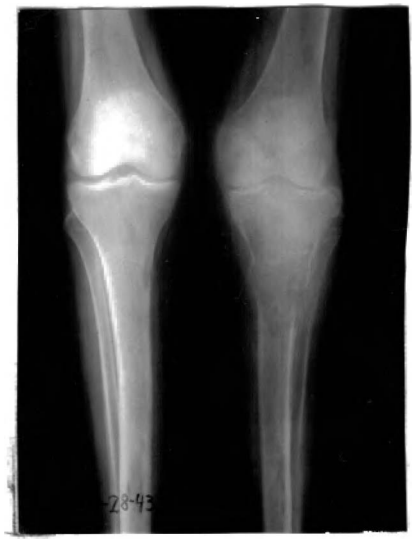
Case No. 2



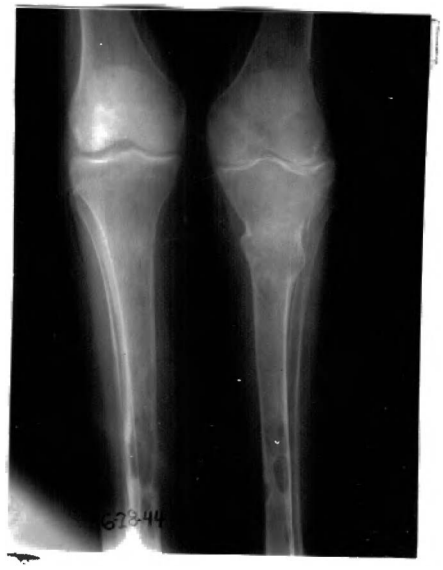
A. 10-15-43



B. 11-43



C. 12-28-43



D. 6-28-44

Mrs. P.S. Age 42.

Clinical summary: Fatigue, loss of energy, failure of appetite. Pain in left leg for 3 months with gradual swelling. Loss of 30 pounds in 6 months. B.P. 180/120.

Laboratory: Blood calcium--13 mg.%. Phos. 2. Phosphatase 7.3 units. P.S.P.- 1st hr. 10%, 2nd hr. 15%--25%.

Pathology: Biopsy taken of tissue from tibia. Reported: grossly, hemorrhagic. Fibrous stroma in which are many foreign body type of giant cells.

X-ray: General demineralization of bony skeleton. Irregular widening of Haversian canals, associated with well circumscribed areas of complete demineralization through the skull and pelvis, tibiae and osseous system in general.

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