THE DIFFERENTIAL DIAGNOSIS OF HYPERPARATHYROIDISM*

WITH SPECIAL REFERENCE TO POLYOSTOTIC FIBROUS DYSPLASIA

(*Lichtenstein—Jaffe*)

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IN THE 12 years that have passed since Mandl, at the suggestion of Erdheim, first removed a parathyroid adenoma in a case of hyperparathyroidism, the number of reported cases of this disease has increased considerably. Up until February, 1936, Wilder and Howell were able to collect 135 cases, which, upon careful analysis, were unquestionably authentic instances of the disease. Undoubtedly, there have been many others which have not been reported.

The clinical, roentgenographic, and chemical aspects of hyperparathyroidism have been stressed so frequently in the past decade that the disease has become familiar to the medical profession at large.

It may be well, however, to again state that the various manifestations of hyperparathyroidism are dependent upon the secretory hyperactivity of one or more parathyroid adenomata which bring about a profound disturbance of calcium and phosphorus metabolism, and that surgical removal of the tumor results in either complete cure or marked amelioration of the symptoms. The disease, which occurs more frequently in females and usually in middle life, is measured, as a rule, in terms of years. It is characterized by bone and joint pain, muscle weakness, localized bone swellings, pathologic fractures, particularly of the extremities and ribs, disturbances of gait, and, in advanced cases, deformities of the bones. There may be other symptoms which become so prominent as to cloud the more important aspects of the clinical picture. These are attacks of intractable nausea and vomiting, polyuria and polydypsia, renal colic, anorexia, severe constipation, loss of weight, and secondary anemia.

The explanation of the roentgenologic findings rests upon a knowledge of the disturbance of physiologic activity of the parathyroid tumor. Normally, it is the function of the parathyroid bodies to control calcium and phosphorus metabolism within the narrow confines of fairly constant blood serum values of 9.5 to 10.5 mg. of calcium per 100 cc. and 3 to 3.5 mg. of phosphorus per 100 cc. When parathyroid activity is increased, because of the presence of a hyperfunctioning tumor, the serum calcium level is increased and the phosphorus decreased due to the fact that greater quantities of calcium salts are withdrawn from the bones. Usually, increased phosphatase activity can be demonstrated. The effect of prolonged withdrawal of calcium salts from the skeleton becomes evident upon roentgenologic examination. The bones of the

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skull present a finely granular appearance. The long bones appear porotic with thinning of the cortex and trabeculae. There may be cyst formation in the center of the shaft. The pelvic bones are frequently cystic. The vertebrae present a coarsely granular pattern similar to that seen in the skull. Due to softening of the skeleton, deformities result from gradual collapse of supporting structures such as the spine, pelvis and thoracic cage.

Up to the present time, most observers have agreed that a diagnosis of hyperparathyroidism should be made when, in addition to the clinical symp-

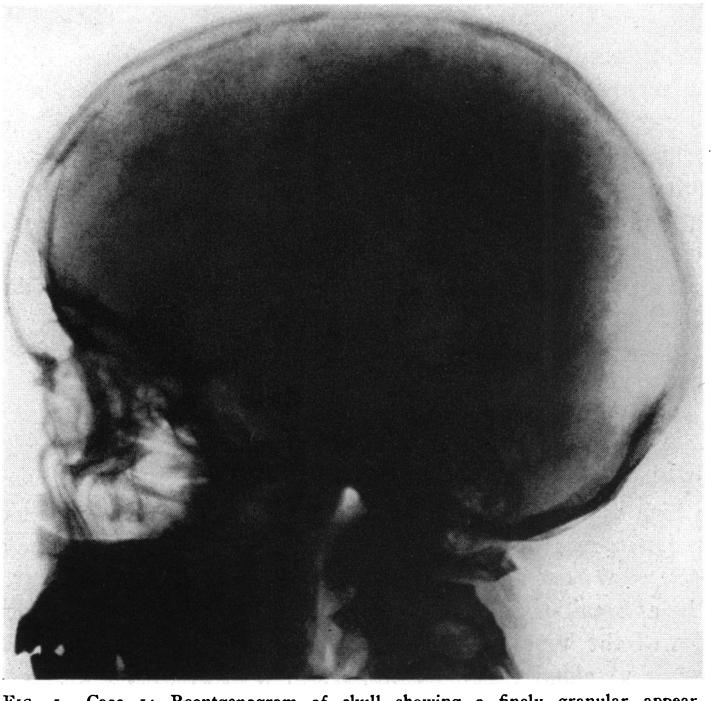

FIG. 1.—Case 1: Roentgenogram of skull showing a finely granular appearance of the bones of the calvarium due to absorption of calcium.

toms and roentgenologic findings already enumerated, there is found a hypercalcemia, a hypophosphatemia, an increase in the serum phosphatase and a proven negative calcium balance. In fact, the combination of these laboratory findings is considered pathognomonic of the disease. However, the course of events and the laboratory findings in Case 3, herewith appended, tend to cast considerable doubt as to the validity of considering these laboratory tests as pathognomonic of hyperparathyroidism. As a result of this experience it may become necessary to reconsider the entire problem in order to establish criteria which would aid in the increasingly difficult aspects of differential diagnosis.

In order to emphasize some of the points to be considered in differential diagnosis, two cases of proven hyperparathyroidism are briefly reported.

Case 1.—M. L., female, age 29, single, referred by Dr. Reuben Ottenberg on March 30, 1937. About 18 months previously, she had consulted her dentist concerning the re-

moval of a tooth. Roentgenologic examination of the jaw at the time showed bony rarefaction involving the maxilla and mandible. A few months later, after a comparatively slight injury, the patient fractured the left patella, which, however, united without much difficulty. About one year ago, roentgenologic examination of the long bones demonstrated small cystic areas in the lower ends of the right radius and ulna. At that time the blood calcium was reported to be 14 mg. per 100 cc., and the phosphorus 2 mg.

A roentgenologic examination of the entire skeleton showed: (a) Marked decalcification of the skull, which presented a sieve-like appearance; (b) the radius and ulna were decalcified, with small cystic areas in the proximal end of the left radius and distal ends of right radius and ulna; (c) the knees showed marked bony absorption in the femora, with cysts in the left patella; (d) the pelvis showed cystic bone absorption in the right ilium and a suspicious area in the left sacrum. Roentgenologic examination of the kidneys showed no calculi (Figs. 1, 2 and 3).

Physical examination was negative. Urine and blood examinations showed no abnormalities. Just previous to admission to the hospital, the serum calcium was 11.8 mg., phosphorus 2.4 mg. and phosphatase 30.5 Bodansky units.

The patient was admitted to the Mt. Sinai Hospital April 7, 1937. Calcium balance studies showed that, after a three-day diet containing 300 mg. of calcium, the excre-

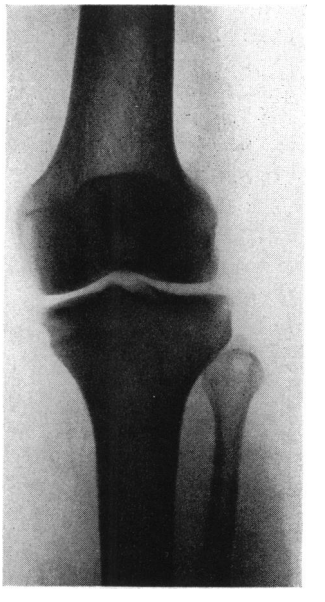

FIG. 2.—Case 1: Roentgenogram of left knee showing cyst in left patella and coarse trabeculation of the femur and tibia.

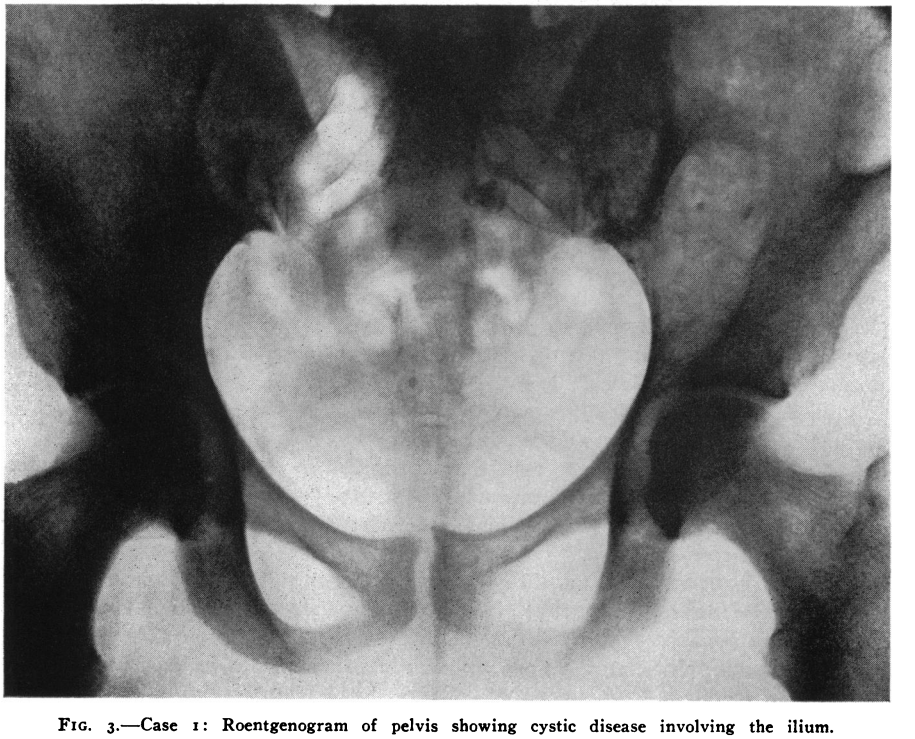

FIG. 3.—Case 1: Roentgenogram of pelvis showing cystic disease involving the ilium.

tion of calcium was 1,073 mg., 771 mg. appearing in the urine and the remainder in the feces. In other words, there was a negative calcium balance of 773 mg.

Operation.—April 13, 1937: A parathyroid adenoma measuring 4.5 by 2 by 1 cm. was found at the lower pole of the right lobe of the thyroid gland (Fig. 4). It dipped downward, behind the sternum, toward the mediastinum. Both sides of the neck were explored, but no other tumors were found. Two normal parathyroid bodies were found on the left side.

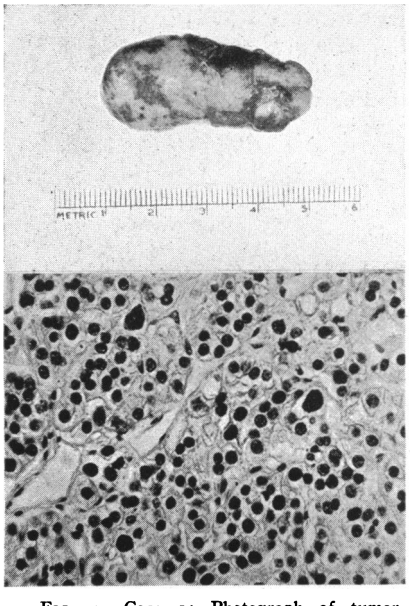

FIG. 4.—Case 1: Photograph of tumor of the parathyroid removed at operation. Microscopic section of it which shows that the tumor was composed mainly of chief cells.

Pathologic Examination of the tumor showed it to be quite cellular. It was composed mainly of pale, water-clear chief cells, with frequent giant cells, and some small groups of oxyphile cells (Fig. 4).

Convalescence was uneventful until the fourth day, when she developed headache, tingling in the face, hands and feet, and diarrhea. There was a positive Chvostek's sign. At this time the serum calcium was 6.9 mg. and the phosphorus 3 mg. This mild tetany responded promptly to parathormone and calcium gluconate. At the time she left the hospital, April 23, 1937, the serum calcium was 9 mg.

Since her discharge, the patient has improved steadily. There has been no recurrence of symptoms and the blood figures are normal. The patient has returned to work.

Case 2.—Hosp. No. 407735: An Italian woman, age 36, was admitted to the Medical Service of the Mt. Sinai Hospital September 8, 1936. For the preceding year she had been receiving treatment in the Out-Patient Department for a right renal calculus. She complained of recurring attacks of pain in the right lumbar region, which had begun four years previously, following a pregnancy. The pain occasionally radiated to the right groin. It was never accompanied by chills, fever or hematuria. The past history was irrelevant.

Physical examination was negative. The blood count was normal, as was also the urinalysis. Blood sugar, 90 mg.; urea nitrogen, 15 mg.; serum calcium, 13 mg.; serum phosphorus, 4 mg. Phosphatase determination showed eight King-Armstrong units. A later blood examination showed the calcium to be 11.8 mg. and the phosphorus 3.5 mg. Roentgenologic examination of the skull and long bones failed to reveal any abnormality. A suspicious rarefied cystic-like area was seen in the left ilium. The patient was discharged September 30, 1936, as a possible case of hyperparathyroidism.

She was readmitted April 26, 1937, complaining that she had been having generalized bone pains for the preceding three months. These were boring in character and involved mainly the left shoulder, knees and hips. She also experienced occasional attacks of nausea without vomiting.

Physical examination was again negative. The roentgenologic examination was repeated and disclosed an enlargement of the previously noted cystic area in the left ilium, as well as the presence of two small calculi in the right kidney pelvis (Fig. 5). Serum calcium, 11.6 mg.; phosphorus, 3.4 mg.; calcium balance studies revealed a daily negative balance of one gram.

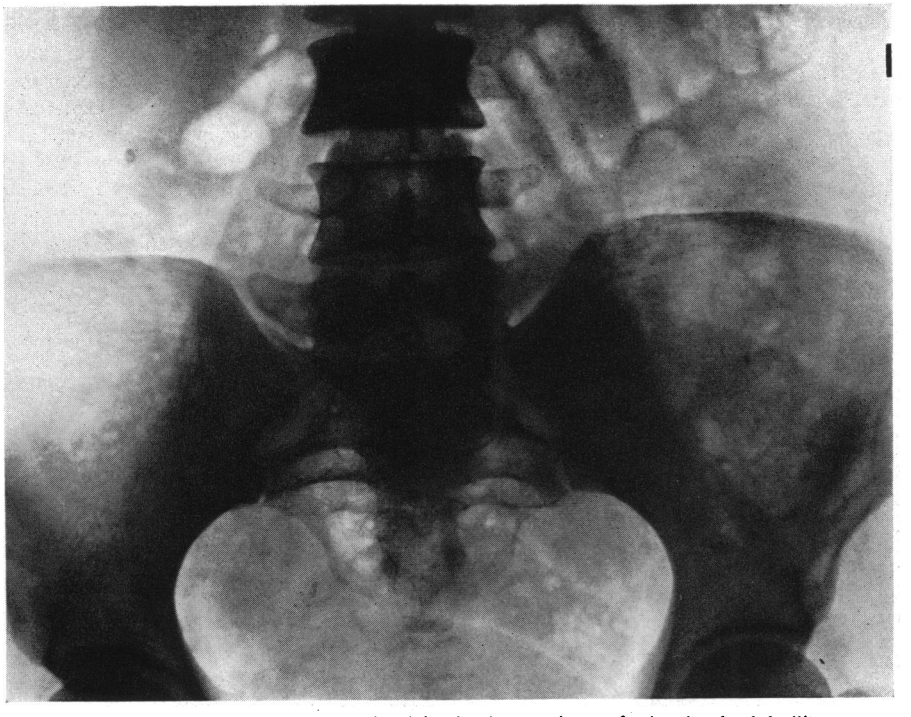

FIG. 5.—Case 2: Roentgenogram of pelvis showing cystic rarefaction in the left ilium.

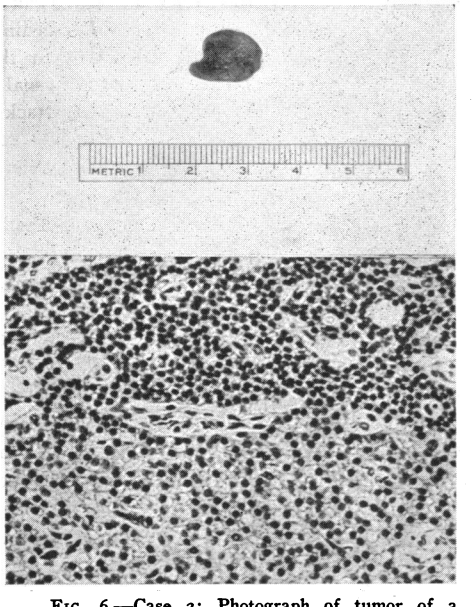

FIG. 6.—Case 2: Photograph of tumor of a parathyroid removed at operation. This represents about two-thirds of the original size of the tumor. Microscopic section of it shows that the tumor was composed mainly of chief cells.

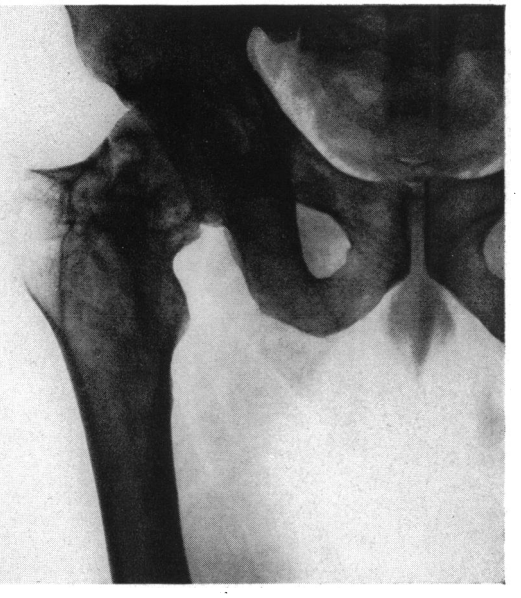

FIG. 7.—Case 3: Roentgenogram of the left hip showing an incomplete fracture of the neck of the femur and the apparent cystic rarefaction of the neck and shaft of the femur.

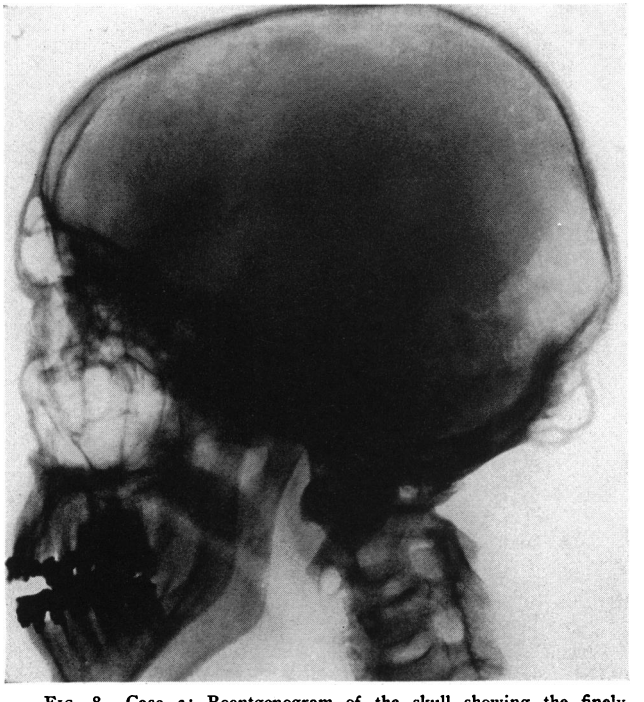

FIG. 8.—Case 3: Roentgenogram of the skull showing the finely granular appearance similar to that seen in Fig. 1. In addition, there is apparent cystic rarefaction of the occipital protuberance.

Operation.—April 30, 1937: Considerable difficulty was encountered in locating the parathyroid adenoma, which was finally found embedded in the substance of the right lobe of the thyroid near its postero-external surface. The adenoma which measured 3 by 2.5 by 1.5 cm., presented the typical reddish-brown color. It was removed *in toto*. Search was made for additional tumors, but none were found. Two normal parathyroid bodies were demonstrated. Histologic examination of the adenoma showed it to be composed mainly of chief cells (Fig. 6).

Convalescence was uneventful other than for the development of a positive Chvostek's sign which persisted for one week. The serum calcium figures were 8.7, 9.7 and 9.1 mg. The patient was discharged May 15 in excellent condition.

When last seen, November 8, 1937, she stated that she no longer had any bone pains and that the pain in the right lumbar region had also disappeared.

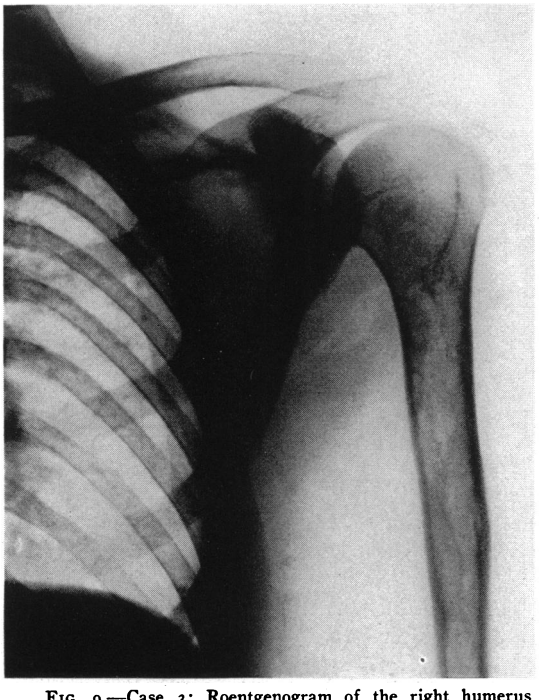

FIG. 9.—Case 3: Roentgenogram of the right humerus which presents an appearance similar to that seen in osteitis fibrosa cystica. Closer examination indicates thinning of the cortex which, on microscopic section, is found to be due to erosion from the endosteal surface. The apparent cystic areas represent fibrous tissue containing islands of immature bone.

In contradistinction to the above cases, I wish to report, in detail, the history of the patient which forms the basis of this paper.

Case 3.—M. S., male, age 47, was seen May 2, 1937 in Richmond, Va., in consultation with Drs. Wm. H. Higgins, Carrington Williams, Bigger and Alice Bernheim. Approximately two months previously, while in England, the patient had developed pain and lameness in the left hip. Three weeks later while playing ping-pong on board ship, he experienced a sudden, sharp pain in the left hip. He was able, however, to carry on his activities, but with some difficulty. Roentgenologic examination demonstrated an incomplete fracture of the neck of the left femur without displacement or impaction (Fig. 7). In addition, there was found an extensive rarefaction of the neck and shaft of the femur

which suggested to Doctor Higgins the possibility of osteitis fibrosa cystica. He was admitted to St. Luke's Hospital, Richmond, for study.

Roentgenologic examination of the remainder of the skeleton disclosed what appeared to be cystic rarefactions in the lower end of the left femur, lower end of right humerus, occipital bone, pelvis and two ribs (Figs. 8, 9 and 10). Blood serum examination showed calcium, 13 mg.; and phosphorus, 2.8 mg. per 100 cc.

On the natural assumption that the patient was suffering from hyperparathyroidism resulting in a pathologic fracture of the left hip, exploration of the neck was undertaken by Dr. Carrington Williams. After a prolonged and thorough search, no parathyroid adenoma was demonstrable. Convalescence was uneventful and the wound healed by first intention.

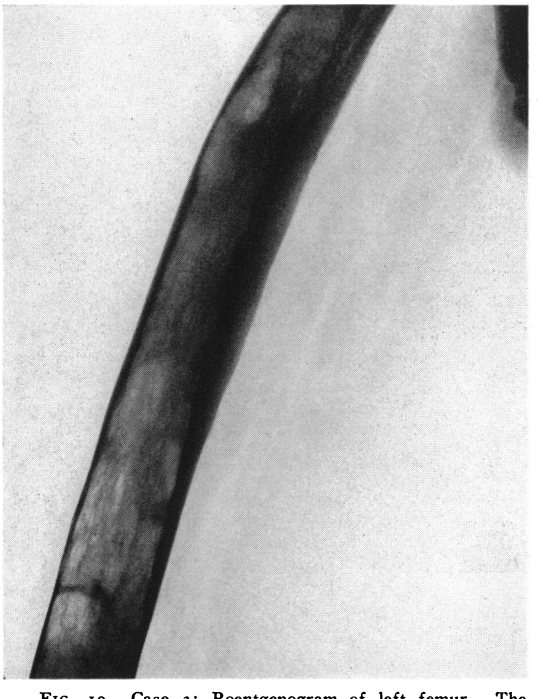

FIG. 10.—Case 3: Roentgenogram of left femur. The findings here are similar to those seen in Fig. 9. They may be easily mistaken for the roentgenologic evidence one sees in cases of osteitis fibrosa cystica.

Careful inquiry into the patient's past history brought out the interesting fact that since childhood the left leg had been one inch longer than the right, and that for the past ten years the patient had had frequent pains in the left thigh and knee.

The patient was transferred to New York in order that careful calcium balance studies might be undertaken in the hope of definitely establishing a positive diagnosis, and entered the New York Hospital May 4, 1937.

Examination was negative except for a prominent occipital protuberance and the fact that the left lower extremity was 3 cm. longer than the right.

Laboratory Data.—Urine, negative; there was no Bence-Jones protein; hemoglobin, 94 per cent; red blood cells, 4,570,000; white blood cells, 8,600; polymorphonuclear leukocytes, 66 per cent; lymphocytes, 19 per cent; monocytes, 11 per cent; basophiles, 4 per cent; serum calcium, 11.3 mg.; phosphorus, 3.2 mg.; and phosphatase, four Bodansky units.

The patient was placed on a three-day diet containing 300 mg. of calcium. During this time, bowel function was normal. The diet was continued for three more days and all urine and feces excreted during this second period were examined for calcium excretion. The measured calcium intake during the initial three-day period obviates the possibility of error from additional calcium which may be present in the intestinal tract. Examination of the stool and urine specimens collected during the second period showed an excretion of 1547 mg. of calcium, 841 mg. appearing in the urine and 706 mg. in the feces. In other words, the patient presented a marked negative calcium balance. This seemed fairly conclusive confirmatory evidence of the existence of hyperparathyroidism.

Before undertaking a second neck exploration, I asked Dr. H. Jaffee to see the patient. After a prolonged examination of the roentgenograms and the laboratory data, he formed the opinion that the evidence was overwhelmingly in favor of a diagnosis of hyperparathyroidism, but reserved a 5 per cent possibility that the patient might be suffering from polyostotic fibrous dysplasia. He concurred in the opinion that the neck should be explored again.

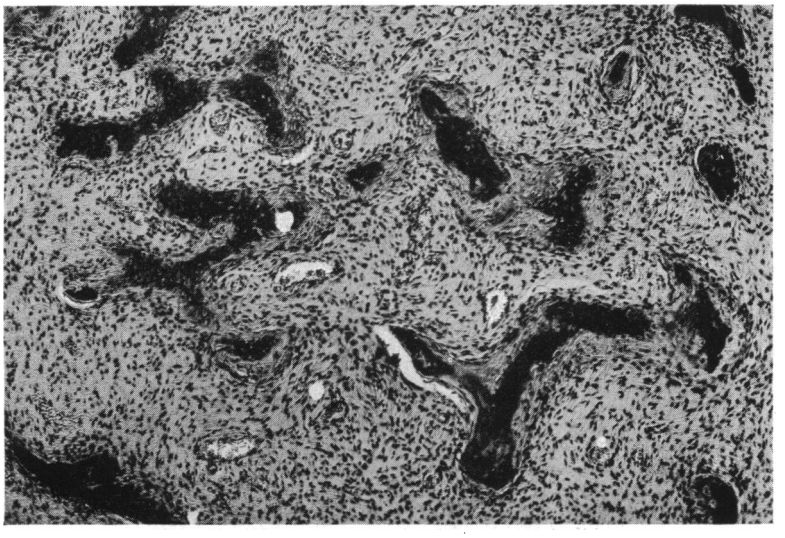

FIG. 11.—Case 3: Microscopic section of the bone biopsy taken from the left femur which shows fibrous tissue metaplasia of the bone marrow containing scattered islands of immature bone. This is one of the characteristic findings of "polyostotic fibrous dysplasia."

Operation.—May 14, 1937: The technical difficulties were considerable because of extensive scarring. A thorough exploration of the neck and superior mediastinum was made, but no parathyroid adenoma was found. The wound was closed. Through a longitudinal incision on the lateral aspect of the left thigh, the upper part of the femur was exposed and a liberal section of cortex and subjacent tissue was removed. The cortex was found to be extensively eburnated and somewhat thinned. The marrow was replaced by dense fibrous tissue which had a rubbery consistency.

Pathologic Examination of the bone biopsy material by Doctor Jaffe showed replacement of the normal marrow by vascular fibrous tissue which contained numerous trabeculae of immature bone (Fig. 11). There were no giant cells and no evidences of active resorption or transformation of the metaplastic new bone. *Diagnosis.*—Polyostotic fibrous dysplasia.

Convalescence was uneventful. The operative wound healed without incident and the patient returned to Richmond the end of May. Repeated roentgenologic examinations of the hip showed subsequent solid union at the site of fracture. At Doctor Bernheim's sug-

gestion the patient was placed on a high calcium and high vitamin diet which he has continued to date. He was advised to avoid undue physical activity in order to guard against possible fracture. He has resumed his business activity and now feels well. A recent check-up roentgenologic examination of the skeleton indicates that some calcification of the involved bones is taking place. The serum calcium is 8.7 mg.; phosphorus, 3.4 mg.; phosphatase, 5.9 Bodansky units.

DISCUSSION.—There will appear in the Archives of Surgery, vol. 36, 874–898, May, 1938, an article by L. Lichtenstein on "Polyostotic Fibrous Dysplasia." The material forming the basis of this paper was assembled in the laboratory of Dr. H. Jaffe at the Hospital for Joint Diseases in New York. The following discussion of the disease is based upon conversations with Drs. Jaffe and Lichtenstein, to whom appreciation is hereby expressed for the privilege of reporting, briefly, the results of their investigations.

The disease, which Lichtenstein gives the name "Polyostotic Fibrous Dysplasia," has been, heretofore, reported in the literature under a great variety of titles, such as "Osteo-Dystrophia Fibrosa Unilateralis," "Unilateral Recklinghausen's Disease," "Unilateral Polyostotic Osteitis Fibrosa," "Focal Osteitis Fibrosa," "Osteitis Fibrosa in Multiple Foci," "Osteitis Fibrosa with Formation of Hyaline Cartilage," "Osteitis Fibrosa Disseminata," *etc.* Lichtenstein and Jaffe have, up to the present time, seen nine instances of the disease, four in their own hospital and five at other institutions, including the case reported in this paper.

A review of the case histories would seem to indicate that the age of onset of symptoms is in childhood or early adolescence, and that females are predominantly affected. The common presenting symptoms are limp, bone pain, deformity of the affected limb and pathologic fracture. It may take years for the disease to progress to a point where medical aid is sought. Our patient was age 47 before severe symptoms developed, although bone pain had been present for the preceding 10 or 12 years.

A peculiar feature is the tendency of the bone lesions to be predominantly unilateral in distribution, either side being affected without preference. Exceptions to this, however, are not uncommon, as is indicated in our own case. Although the femur and tibia are most frequently involved, it is not unusual to find evidences of the disease in the radius and humerus as well. The skull and pelvis may also be affected.

The characteristic findings on roentgenologic examination may be summarized as follows: (1) Broadening or expansion of the bone; (2) thinning of the cortex; (3) characteristic rarefied and apparently trabeculated appearance; (4) secondary deformities of the affected bones. Pathologic fracture of the neck of the femur is common. Inasmuch as the condition is frequently erroneously interpreted as osteitis fibrosa cystica, or Recklinghausen's disease, it is important to examine the entire skeleton roentgenologically in order to determine whether the bone lesions are unilateral in distribution. This is an important point in differential diagnosis. As will be pointed out, the bones involved in polyostotic fibrous dysplasia do not contain cysts, in contradistinc-

tion to hyperparathyroidism, and this must be borne in mind when interpreting the roentgenograms.

The basis of Lichtenstein's interpretation of the pathologic features of the disease is adequate biopsy material obtained from nine cases. The bone cortex is considerably thinned out, due in part to resorption, but largely to erosion of the endosteal surface by the proliferating fibrous tissue replacing the marrow cavity. There is no evidence of periosteal proliferation or new bone deposition. The medullary cavity is filled with fibrous tissue which is grayish-white in color and has a peculiar consistency described as spongy or rubbery. It has also been noted to be gritty. This fibrous tissue is composed of spindle cells with oval, pale staining nuclei. In some areas the basic connective tissue has undergone a fibroblastic differentiation into mature connective tissue containing a large amount of collagen. Dispersed irregularly in this fibrous tissue may be seen small trabeculae of primitive, poorly calcified new bone. The fibrous tissue appears relatively avascular. There may be seen small nests of giant cells, resembling osteoclasts. Occasional islands of hyaline cartilage may be found within the fibrous tissue. This is not a constant finding.

I wish to quote verbatim from Lichtenstein's paper in order to express his views on the pathogenesis of this disease: "The characteristic pathologic feature of polyostotic fibrous dysplasia appears to be a disturbed function or development of the bone-forming mesenchyme, which results in replacement of the spongiosa and filling of the medullary cavity of affected bones by fibrous tissue in which trabeculae of poorly calcified primitive new bone are developed by osseous metaplasia. The seemingly complex histologic picture becomes much easier to interpret if one predicates the multipotential capacity of this undifferentiated fibrous tissue. The latter normally gives rise to the spongiosa and to the myeloid or fatty marrow, but under pathologic conditions it may develop in several anomalous ways. By osseous metaplasia, it gives rise to osteoid and primitive fiber bone. By cartilaginous metaplasia, it gives rise to sporadic, isolated islands of hyaline cartilage, which tend to become calcified. By fibroblastic differentiation, it gives rise to mature collagenous connective tissue. Finally, by coalescence of its nuclei, it may give rise to multinuclear cells, indistinguishable from osteoclasts. Whatever stimulates the continued perverted activity of the undifferentiated fibrous bone-forming mesenchyme, or initiates the disorder remains a matter of conjecture. The clinical history of symptoms dating back to early childhood strongly suggests a congenital basis for this curious anomaly."

In Lichtenstein's series, serum calcium determinations ranged between 9.8 and 11 mg. per 100 cc. The serum phosphorus estimations showed no significant change. In three of his cases, the phosphatase was considerably increased; namely, 17, 18 and 22 Bodansky units. Lichtenstein feels that the increased phosphatase values in polyostotic fibrous dysplasia afford additional evidence to support the contention of Bodansky and Jaffe that the activity of the enzyme phosphatase is proportional to the stimulus to new bone

formation. It is interesting to note that the serum values of the patient reported in this paper were such as to confuse the diagnostic problem considerably. In Richmond, the serum calcium was 13 mg. and the phosphorus 2.8 mg. When these were repeated in Bernheim's laboratory at the New York Hospital, they were 11.3 mg. of calcium and 3.2 mg. of phosphorus. The phosphatase determination was four units.

In none of the cases studied at the Hospital for Joint Diseases were calcium balance studies made. In our own case, such studies showed an excretion of 1547 mg. of calcium in the urine and feces over a three-day period, during which a measured diet containing 300 mg. was ingested. This indicated a

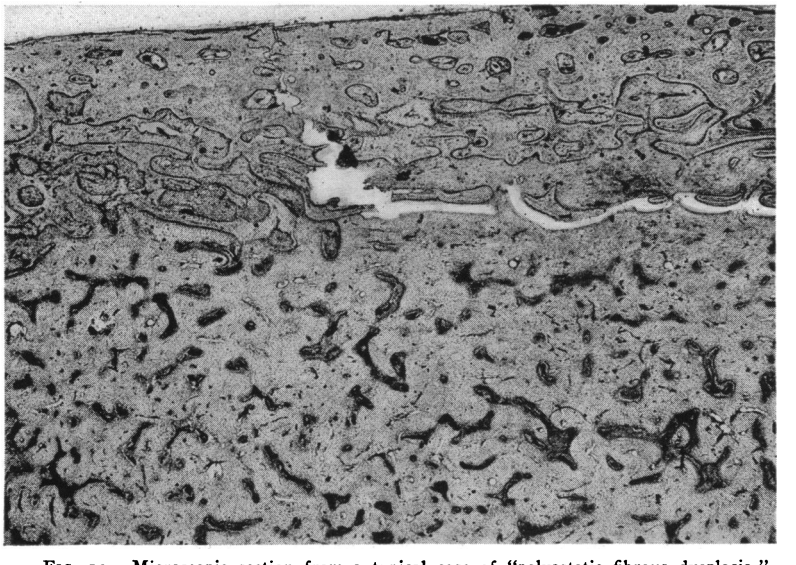

FIG. 12.—Microscopic section from a typical case of "polyostotic fibrous dysplasia," showing the fibrous tissue filling the medullary cavity and thinning of the bone cortex due largely to erosion of the endosteal surface. Dispersed irregularly in the fibrous tissue are small trabeculae of primitive poorly calcified new bone. (From the collection of Dr. Henry Jaffe, Hospital for Joint Disease, New York.)

marked negative calcium balance which, in conjunction with all other findings, was considered conclusive evidence of an existing hyperparathyroidism.

The importance of the laboratory and roentgenologic findings in Case 3 now becomes obvious. It is evident that a patient with polyostotic fibrous dysplasia may present all the clinical and confirmatory laboratory evidence usually associated with hyperparathyroidism, or osteitis fibrosa cystica.

CONCLUSIONS

It is suggested, therefore, that the surgeon, when confronted with suspicious bone lesions evident in the roentgenograms, and serum estimations of calcium and phosphorus which are outside the normal limits, and in spite of the fact that calcium metabolism studies may show a negative balance, should not be too hasty to advise exploration of the neck for a parathyroid adenoma. It is suggested further that, when doubt exists as to the diagnosis, additional

investigation should be undertaken to clarify the situation. This consists, first, of roentgenologic examination of the skeleton to determine whether the bone lesions have a predominantly unilateral distribution and second, the performance of a bone biopsy. The latter will definitely establish the diagnosis by differentiating the characteristic histologic pictures of polyostotic fibrous dysplasia and hyperparathyroidism (Figs. 12 and 13).

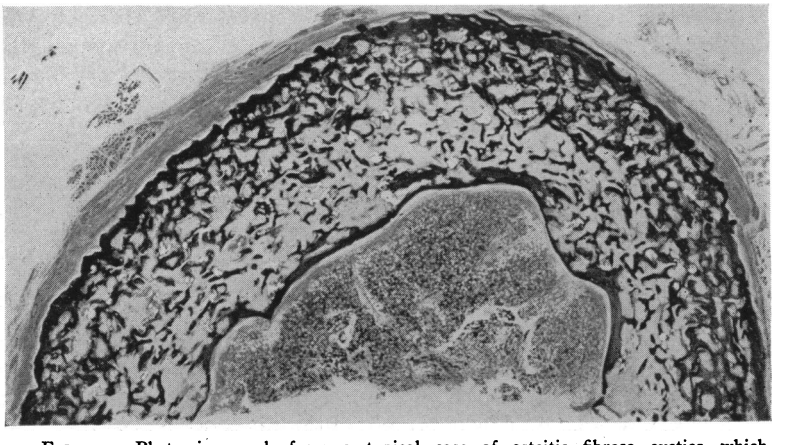

FIG. 13.—Photomicrograph from a typical case of osteitis fibrosa cystica which should be compared with Fig. 12. This indicates that most of the bone change has taken place in the cortex with cystic degeneration and bone absorption as the predominant features. There is little or no change in the medullary cavity. (From the collection of Dr. Henry Jaffe, Hospital for Joint Disease, New York.)

DISCUSSION.—DR. EMIL GOETSCH (Brooklyn) said that Doctor Garlock had drawn attention to some very interesting as well as anomalous conditions which simulate parathyroid dysfunction but which are not due to parathyroid hyperactivity. The present status of knowledge concerning the parathyroid is rather confused but, as with previous clinical syndromes, the time will come when those due to parathyroid dysfunction will be more clearly differentiated.

The first two cases were unusually illustrative of the clinical conditions typical of parathyroid adenomatous tumors. There were the usual blood changes with elevation of the calcium level and a diminution in the phosphorus content. There was an increase in the phosphatase and the bone changes first described by von Recklinghausen were typical of those found in instances of hyperactivity of the parathyroid. It is very satisfactory to have found parathyroid adenomata with the establishment of the real cause of the disease, and it is very satisfactory to have obtained such good results after the removal of the parathyroid tumors. Incidentally, too, the calcium and phosphorus content of the blood returned to normal, and there was an improvement in the condition of the bones due to redeposition of calcium in those areas from which calcium had been absorbed.

The third case was rather troublesome in that the bone changes were certainly suggestive of those found in hyperparathyroidism and there was associated a negative calcium balance, an association of findings very suggestive of parathyroid tumor. After most careful search, no parathyroid tumor or adenoma was found. Doctor Garlock called attention to the disease designated as "polyostotic fibrous dysplasia" which exhibits the findings just described and warned against being too hasty in operating for a supposed instance of

parathyroid tumor even in the presence of a negative calcium balance and rarefaction of the bones.

The last case further demonstrated the great value of calcium balance studies and that one cannot rely upon blood calcium findings alone. Calcium balance determinations over the three-day period are far more valuable than a few isolated blood calcium determinations. Thus, a high calcium change may be present due to failure of excretion or, on the other hand, a relatively low calcium may be present in instances of rapid excretion. The value of calcium balance determination, therefore, is obvious. Doctor Garlock warned against too prompt exploration of the neck before a very careful clinical investigation has been made. Too many conditions in which calcium deposits have been found, such as arthritic changes or arteriosclerosis, have been attributed to parathyroid dysfunction. Even scleroderma or arteriosclerosis has been attributed to disturbances of parathyroid function. In a recent case of this kind with extensive sclerosis, stiffness of the face and "wooden" fingers, Doctor Goetsch was prevailed upon to explore for parathyroid tumor but after most careful search nothing was found, although there was present an interesting generalized fibrous sclerosis, deep as well as superficial. Incidentally a small isolated tumor of thymus tissue was found at the right lower pole. At times it is difficult to identify, absolutely, parathyroid tissue for it may be atypical and thus be confused with the appearances commonly noted in true lymph nodes or hemolymph nodes commonly found in the region of the parathyroids. Also there may be an admixture of lymphoid tissue. Illustrations are sometimes exhibited which appear more like lymphoid tissue than true parathyroid tissue.

DR. HENRY L. JAFFE (New York) thanked Doctor Garlock for his generous acknowledgment of the work of Doctor Lichtenstein and himself in connection with "polyostotic fibrous dysplasia," the pathology of which they had been able to clarify on the basis of cases coming under their observation, which helped to establish it as an entity.

A number of points bear reemphasis. One rarely observes a clear-cut increase in the serum calcium value in "polyostotic fibrous dysplasia." Of the cases observed by Doctor Jaffe only two had figures above 11, and those figures were below 11.5 mg. per 100 cc. The serum phosphorus figures (which are also important in the diagnosis of true cases of hyperparathyroidism) were more or less normal in all the cases observed. The serum phosphatase activity values were high except in one case, and that was a man of 47. His biopsy specimen showed relatively little new bone in the fibrous tissue filling the marrow cavity and, furthermore, there was not very extensive involvement in his case. In younger subjects, with more extensive lesions, the phosphatase values were high and, indeed, as high as in hyperparathyroidism.

The marked negative calcium balance reported by Doctor Garlock threw Doctor Jaffe off altogether. On empiric grounds he could not believe that cases of "polyostotic fibrous dysplasia" should show pronounced negative calcium balances. In fact, he considered making calcium balance studies on several of his cases, but since the osseous involvement was not generalized and was often quite limited, he felt certain that the calcium balance studies would show nothing remarkable. It is true that Doctor Goetsch emphasized the value of calcium balance studies and many people have been stressing their value in diagnosis of various skeletal diseases. Nevertheless, Doctor Jaffe doubted the value of the information obtainable from a three-day calcium balance study as done by present methods. The fact is that a normal person on a diet containing 100 mg. of calcium shows in a three-days' balance study a negative calcium balance and the calcium balance studies only measure the degree of negativeness from person to person. Doctor Jaffe did not doubt Doctor Bernheim's figures for Doctor Garlock's case, yet he was skeptical

that subjects with "polyostotic fibrous dysplasia" show pronounced negative balances. He emphasized that it is of the utmost importance to clarify this point in the differential diagnosis between this condition and hyperparathyroidism. Certainly if studies of additional cases show that the calcium balance is severely negative, then there is another confusing point in the differential diagnosis between it and hyperparathyroidism. Doctor Jaffe hoped for the sake of diagnosis that it would prove to be otherwise.

Regarding roentgenologic findings, Doctor Jaffe affirmed Doctor Garlock's statement that there is a tendency for the lesions to be unilateral. Furthermore, the lesions, statistically, tend to concentrate in the femur and tibia, although he had seen them in the calvarium and particularly in the occipital bone, also in the ribs, in the vertebrae, in the pelvic bones, and even in the small bones of hands and feet. The reason why cases of "polyostotic fibrous dysplasia" are misdiagnosed as hyperparathyroidism is that the fibrous tissue growing in the marrow cavity erodes the inner surface of the cortex and may even distend the bone, and, of course, the bone shadow is suggestive of a cyst. Actually these bones are not cystic. When one penetrates the cortex, one finds the marrow cavity filled by a hard and almost rubbery tissue. Even where the picture is, roentgenographically, clearly that of a cyst, this type of tissue exists.

One important point in the roentgenologic differential diagnosis between "polyostotic fibrous dysplasia" and hyperparathyroidism is rarefaction of the cortex of most bones in the latter and the absence of cortical rarefaction except in the affected bone in the former.

DR. CARL G. BURDICK (New York) asked Doctor Jaffe regarding the outcome of some of the cases he had followed.

DOCTOR JAFFE answered that the first case he saw was a girl who at the time of his first observation (1926) showed involvement of a number of ribs, one femur, and one tibia. She had a fracture through the neck of the femur. She left the Hospital for Joint Diseases and some years later Doctor Jaffe traced her to Long Island College Hospital where a bone graft had been inserted in the femur. She became a mother of two children and her illness was not particularly aggravated by the pregnancies. She still has the disease and presumably she will go on having it. Some of the lesions may subside somewhat as she becomes older. The fibrous tissue may become more collagenous and the condition consequently less progressive.

DR. BRADLEY L. COLEY (New York) recalled a case of malignant tumor of the parathyroid gland which he showed before the New York Surgical Society in 1936. At that time it was assumed that the changes in the patient's spine, which originally brought him under Doctor Coley's care, were due to hyperparathyroidism associated with the tumor. The subsequent course, however, proved that the lesion in the spine was really a metastasis, and when last seen the patient was growing rapidly worse. In retrospect, the case represents one of malignant tumor of the parathyroid (adenocarcinoma of parathyroid origin) with metastasis to the lumbar spine.

DR. JOHN H. GARLOCK (New York), in conclusion, said that Doctor Jaffe's remarks about calcium balance studies were very well taken. Nevertheless, he could not alter his belief in Doctor Bernheim's figures. Doctor Bernheim has done many calcium balance studies over a long period of time in her own laboratory in New York Hospital, and also has a technician who has been working under her for many years, and knows how to carry out the studies. In the case presented these studies definitely showed a marked negative calcium which Doctor Garlock considered to be a very important finding.