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Boy Frame

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PHOSPHATE DIABETES
A REVIEW

GEOFFREY FALKSON, M.B. Ch.B* AND BOY FRAME, M.D.*

Phosphate diabetes is the term proposed by Fanconi for the clinical entity otherwise known as vitamin D resistant rickets. Most of the information regarding this condition has been gained by the study of individual cases. Its infrequent occurrence has prevented a cumulative experience by any one group. Larger series have been studied for the most part when the disease presented a familial incidence. The most complete clinical studies have been performed by Swoboda, who reports 11 cases, and by Tobler working with Prader and Taillard, who report 16 cases. This paper is a review of data obtained from approximately 150 of the more detailed case reports in the world literature and was prompted by the study at this hospital of a patient with severe osteomalacia due to phosphate diabetes.

Since the description of the familial occurrence of tardy rickets by Baagoe and of similar cases resistant to the usual dosage of vitamin D by Jampolis and Londe, interest has been stimulated in rickets and osteomalacia not complicated by demonstrable renal disease or intestinal mal-absorption, yet resistant to average doses of vitamin D. In 1937, Albright demonstrated in phosphate diabetes the ability of vitamin D in massive doses to overcome what he referred to as an intrinsic resistance to vitamin D. It soon became apparent that despite the clinical remission achieved with massive vitamin D therapy, the fasting serum inorganic phosphorus level remained depressed in many instances, suggesting that the disease was not due to vitamin D resistance alone. Robinson, Harris and McCune postulated that primary renal hyperphosphaturia, as demonstrated by the decreased tubular reabsorption of phosphorus, may explain the pathogenesis of the disorder. This concept was opposed to Albright's stand that the hypophosphatemia in phosphate diabetes resulted at least in part from secondary hyperparathyroidism. Either concept may account for the reduced tubular reabsorption of phosphorus and depressed serum inorganic phosphorus found in phosphate diabetes.

Fanconi defined phosphate diabetes as including all cases of osteomalacia without other renal lesions or intestinal mal-absorption and having the following characteristics: 1. Familial, usually with a dominant genetic pattern. 2. Chronic absolute vitamin D resistant hypophosphatemia. 3. Elevated alkaline phosphatase before vitamin D therapy. 4. Normal or hyperphosphaturia, high phosphate clearance, and only minimal increase in phosphate excretion during the Ellsworth-Howard phosphaturia test. 5. Pronounced hypocalciuria. 6. Appearance after the first year. 7. Retarded growth with a sturdy body configuration.

Dent considers that phosphate diabetes is a unifactoral renal tubular defect leading to hyperphosphaturia and osteomalacia. A multi-factoral tubule defect when present would then result in the more complicated conditions of renal tubular acidosis and the Fanconi syndrome, which may also be associated with osteomalacia.

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**Phosphate Diabetes**

**REVIEW OF CASES.**

Few cases of phosphate diabetes reported in the literature have been sufficiently investigated to completely fulfill Fanconi's criteria. We have chosen patients for review in whom, as far as can be determined, there was no question concerning the diagnosis of rickets or osteomalacia from a clinical and biochemical standpoint. Cases with steatorrhea or evidence of a more advanced renal tubular abnormality, manifested as renal tubular acidosis or Fanconi's syndrome, were excluded. All cases showed moderate or marked resistance to treatment with vitamin D. In only a few cases was sufficient study of the urinary phosphorus excretion available to determine whether this was above normal. Since, however, there is strong evidence that primary renal hyperphosphaturia is the main pathogenic defect the collected cases have been grouped under the heading, renal phosphate diabetes. We suspect that many if not all the cases of vitamin D resistant rickets reported in the world literature are examples of phosphate diabetes. This may be in error since there is no absolute proof that a common etiology is present in all cases. Of approximately 180 available cases we consider the data adequate in only 150.1,3,5,7,9,11,13-25,27,28,36,37,50-84. A statistical analysis would have little meaning because of variation in method of reporting the clinical data; therefore many of the conclusions in this report are derived from the study of the individual case reports.

There is a positive family history of the disease in a large number of patients. There are 50 families on record with more than one member affected. Pedersen was the first to draw attention to this clinically significant fact. Mitchell and Mitchell on the basis of a family history involving five generations were able to postulate that the disease is due to a single dominant autosomal gene of variable expressiveness.

The youngest case of phosphate diabetes on record was an infant of 7 months described by Harrison. Since the patient's mother had an inactive form of the disease, its presence in the infant was suspected from birth. The majority of patients with the disease fall between the ages of 1½ and 16 years of age. The oldest patient with active disease at the time of diagnosis was 57 years old, and gross deformities had been present for many years prior to the diagnosis. The incidence of active phosphate diabetes is less in adults, there being on record only 12 patients in whom the disease had its onset after the age 14. Since 60 per cent of the cases were females and 40 per cent males, there appears to be no striking sex predominance.

The clinical picture of phosphate diabetes has been described adequately in many of the individual case reports, especially when it has occurred in childhood. A child's first attempt to walk often calls attention to the disease since gradual convex curving of the thighs or genu valgus may appear early. The gait may be waddling and at times suggestive of that seen in muscular dystrophy. General weakness is sometimes present, but true muscle hypotonia is less common than in classical deficiency rickets. The general condition otherwise may be quite good. When the disease occurs in infancy and childhood, there may be relatively little bone pain and tenderness despite rather severe skeletal deformity. Of unknown significance is the association of phosphate diabetes and a number of seemingly unrelated anomalies. These include albinism, mental deficiency, neurofibromatosis and craniostenosis.

The serum chemistry is similar to that found in vitamin D deficiency rickets. The serum calcium is usually normal, but occasionally slightly depressed. Among the cases
reviewed the highest serum calcium was 11.3 and the lowest, 7.5 mgm. per cent. The average serum calcium for the cases was 9.8 before and 10.8 mgm. per cent during treatment. Persistent hypophosphatemia, considered one of the hallmarks of the disease, is present in almost all cases. The lowest serum inorganic phosphorus value reported was 0.17 and the highest, 7.2 mgm. per cent. The average serum inorganic phosphorus in all cases was 2.5 before and 3.5 mgm. per cent during treatment with vitamin D bordering on toxic levels. Considering the large number of infants and young children in this series, we consider the value of 3.5 mgm. per cent to be lower than normal. The alkaline phosphatase is generally elevated, but there are documented cases in the active phase of the disease with a normal value. In pure phosphate diabetes the serum electrolytes will be normal and the 24 hour urinary calcium depressed.

Increased amounts of glucose and amino-acids will not be present in the urine unless there is a more extensive renal tubular defect. By definition, the term pure phosphate diabetes would no longer apply. Dent, however, using paper chromatography, found an increase in urinary glycine excretion in patients with phosphate diabetes resulting in what he calls the "superglycine" spot. Since the urinary phosphorus excretion in phosphate diabetes has received attention only in recent years, relatively little data is available in the literature for analysis. Further work is needed to evaluate the various factors that control excretion of phosphorus in the urine, both in terms of quantitative values and in terms of the various phosphorus reabsorption tests. A number of authors have studied this problem in patients with phosphate diabetes. Increased urinary excretion of phosphorus has been found in a high percentage but not in all patients with the disease. However, considering the low serum inorganic phosphorus, a normal value for urinary phosphorus excretion may indicate in actuality an excessive loss. In some cases of phosphate diabetes, this excretory rate has continued even after fasting when the serum inorganic phosphorus had fallen almost to zero.

Roentgenograms of the reported cases in childhood simulate those of florid deficiency rickets. There is generalized demineralization of bone and unusually prominent bony trabeculae. The metaphyses of the long bones are broad and frayed, while changes in the spine occur less frequently. The lamina dura is intact unless the bone changes are extremely severe.

We have been particularly interested in clinically active phosphate diabetes as manifested in late adolescence and adulthood. Heretofore, the greatest emphasis has been placed on its occurrence in infancy and childhood. It cannot be said with certainty that the adult form is the same disease or has the same pathogenesis as that found in childhood, but many of the features are similar. As far as can be determined, the nature of the underlying bone disease is identical. In infancy and childhood, due to the unclosed epiphyseal discs, the picture is that of rickets, while after closure of the discs adult osteomalacia is the result. In both instances, poorly calcified bone matrix is the basic abnormality. Hypophosphatemia, both before and after treatment usually occurs in adult cases as well as in childhood. When the disease begins in childhood it frequently becomes inactive and stationary as growth ceases, but the bone deformities
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and hypophosphatemia remain into adulthood. The alkaline phosphatase in these adult cases is frequently normal. We have not considered such adult cases to have active phosphate diabetes. On the other hand, we have found reports of approximately 11 cases in which the disease had its onset during or after adolescence and which continued in a progressive fashion until treatment was instituted. These are included in Table I. As far as could be determined there was no definite family history of rickets or osteomalacia in any of the cases, in contrast to the high familial incidence of the childhood form of the disease. Bone pain, tenderness and moderate muscular weakness, seldom complaints in children with the disease, are prominent features in adult cases. A loss in height of 4-6 inches in adults with the disease is common. The x-ray picture in the adult shows no metaphyseal change but pseudofractures occur often. The latter are rare in the childhood form of the disease.

The treatment of phosphate diabetes is not entirely satisfactory. Untreated children reach adult life with gross bony deformities and are dwarfed. There is recorded only one patient whose disease, having begun in childhood, remained active after growth had ceased. On the other hand, when the onset is in the adult there is more apt to be steady progression. For many years treatment has consisted of massive doses of vitamin D and calcium supplements. Since most of the cases were started on very large doses of the vitamin as soon as the diagnosis was established, it is impossible to determine the minimal amount necessary to produce improvement. In the cases reviewed, no clinical improvement was achieved on less than 10,000 units of vitamin D daily, while some patients required as much as 1,500,000 units daily. A limiting factor in such therapy has been toxicity to the vitamin, in some cases resulting in intolerable hypercalcemia which occasionally necessitated reduction in dosage to an ineffective level.

The use of added oral phosphorus in the treatment of phosphate diabetes has been emphasized recently. Saville demonstrated increased calcium and phosphorus retention in patients with the disease who were given such treatment. In another recent case report there was striking clinical and radiologic improvement after the addition of 2 to 3 grams of oral phosphorus daily, whereas treatment with large doses of vitamin D and calcium alone during the previous five years had resulted in only minimal improvement. If the hypothesis is correct that phosphate diabetes is at least partly a consequence of negative phosphorus balance due to primary hyperphosphaturia, the use of oral phosphorus supplements seems physiologically sound.

Many patients with phosphate diabetes have been followed in orthopedic clinics for a number of years with the erroneous diagnosis of osteodystrophy and as a result osteotomies were performed to correct the bony defect. If the diagnosis of phosphate diabetes has been correctly established and large doses of vitamin D already initiated, this must be discontinued while the patient is undergoing various orthopedic corrections. Otherwise, immobilization in addition to the high dose of vitamin D, may result in dangerous hypercalcemia and nephrocalcinosis.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of phosphate diabetes includes a variety of diseases. Other forms of rickets and osteomalacia must be excluded. It differs from classical
deficiency rickets not only in that there is resistant hypophosphatemia, family predisposition, the spontaneous occurrence at any age, and relative vitamin D resistance, but also in that continued intensive therapy is necessary without assurance of cure. Mal-absorption syndromes with resulting osteomalacia should be differentiated by appropriate studies. Hypophosphatasia, a recently described syndrome simulating rickets from the radiologic and pathologic aspect, is identified by the markedly depressed serum and tissue alkaline phosphatase. The more extensive renal tubular defects with associated osteomalacia, such as tubular acidosis and the Fanconi syndrome, may be differentiated by the presence of systemic acidosis in the former and aminoaciduria as well as glucosuria in the latter. In actuality, the hyperphosphaturia in Fanconi's syndrome might also be labeled phosphate diabetes, but there are sufficient additional features to keep this entity separate from pure phosphate diabetes. Little difficulty is encountered in differentiating hyperparathyroidism and osteoporosis. The hypercalcemia and hypercalciuria in the former and the normal serum phosphorus in the latter are usually sufficient.

Dwarfism and deformed extremities in phosphate diabetes have often resulted in a diagnosis of osteodystrophy or chondrodystrophy. However, in these diseases the serum calcium, phosphorus and phosphatase, are almost always normal and there is no evidence of hyperphosphaturia. There are a number of non-rachitic varieties of crural varus and valgus that have in the past been confused with the bony deformities of phosphate diabetes. Many of these latter patients have had one or more osteotomies for correction of the deformities without recognition of the underlying metabolic defect. When Pedersen reviewed such cases in his clinic, a surprising number of patients with phosphate diabetes were uncovered.

PATHOGENESIS

The pathogenesis of phosphate diabetes is still to be completely elucidated. For many years the resistance of the disease to the usual doses of vitamin D led to the term vitamin D resistant rickets or osteomalacia. This term was strengthened by the fact that many patients so diagnosed responded to vitamin D only in doses bordering on toxic levels. There are several features which indicate that simple resistance to the vitamin is not the most likely explanation for the condition.

One of the strongest arguments that more than a vitamin resistance is involved is the repeated observation that the vitamin D required for improvement in phosphate diabetes calls forth a different set of responses from those occurring during the treatment of deficiency osteomalacia. With a therapeutic response in the latter, one of the early changes is a prompt elevation of the fasting serum inorganic phosphorus. This is due to increased absorption of phosphorus from the intestine as well as to its improved renal tubular reabsorption. This elevation of serum inorganic phosphorus aids prompt ossification of poorly mineralized bone matrix. Enhanced absorption of calcium is an additional factor in the accelerated ossification. It is true that excessive doses of vitamin D used in the treatment of phosphate diabetes will also improve intestinal absorption of calcium and phosphorus. In this instance, however, a low serum inorganic phosphorus often persists despite the fact that radiologic studies may show healing of the osteomalacia. The fact that vitamin D returns the serum inorganic phosphorus to normal is the primary criterion for the diagnosis of phosphate diabetes.
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phosphorus to normal in simple vitamin deficiency osteomalacia, but only infrequently in phosphate diabetes with osteomalacia, suggests a different mechanism of action of the vitamin in the two diseases. In the former its action may be physiological in nature, while in phosphate diabetes a pharmacological action may affect ossification of bone without affecting the internal homeostasis of phosphorus. Further biochemical differences between these two diseases entities are demonstrated by healing properties of dihydrotachysterol in phosphate diabetes, but not in deficiency rickets. If the same biochemical system is at fault in deficiency osteomalacia as in phosphate diabetes (vitamin resistant osteomalacia) these variances in response to vitamin D and dihydrotachysterol are difficult to explain. Despite the fact that in normal individuals excess vitamin D tends to cause demineralization of bone, this action is not seen in phosphate diabetes. This again suggests that the action of vitamin D is not physiological in the latter condition. The relative hyperphosphaturia seen in phosphate diabetes but not in deficiency osteomalacia also points to biochemical dissimilarities. If the two conditions were basically the same disease process, except for the wide dosage difference in response to vitamin D, we suggest that there would not be these striking disparities either before or after the administration of the vitamin. Contrary to this reasoning, Freeman and Dunsky concluded in 1950 that with massive vitamin D therapy one effect of vitamin D may be accentuated without a second effect being influenced and yet, clinical healing achieved. Harrison's concept of the involvement of two different biochemical systems being affected at the two extremes of dosage is an interesting consideration in this regard. It is also pertinent to ask why a resistance to vitamin D is not apparent in the first few months of life if this is the only etiologic factor in phosphate diabetes. In no case described in the literature has an allergic or hypersensitivity reaction to the vitamin been described which might account for an acquired resistance.

Since we believe that the disease is not simply due to a resistance to the action of vitamin D, we prefer the term proposed by Fanconi and others of primary renal phosphate diabetes. This implies a relative increased phosphorus excretion in the urine. To demonstrate an absolute increase in urinary phosphorus excretion in the disease is difficult due to the problem of controlling the many factors that regulate its total excretion. However, with the use of renal tubular phosphorus reabsorption tests, renal clearance of phosphorus has been shown to be increased in a number of instances of phosphate diabetes. Winberg and co-workers, on the other hand, associate this high renal phosphorus clearance with an increasing dietary content of phosphorus and propose that these are proportional. Thus they rejected the term phosphate diabetes and continue to prefer the term “primary vitamin D refractory rickets”. The proponents of the existence of an increased renal phosphorus clearance in the disease suggest that the main defect is due to either a congenital or an acquired renal tubular defect. Evidence of a primary tubular defect in phosphate diabetes is supported by the fact that there are reported gradations from true phosphate diabetes to the more generally accepted renal tubular defect found in the Fanconi syndrome. The combination of hyperphosphaturia and amino-aciduria, as well as hyperphosphaturia and glucosuria, have been reported in separate cases. This evidence suggests that the eventual clinical manifestations depend upon the degree of renal tubular dysfunction. It has been suggested that an enzymatic defect in the tubules may be primary in the deficient
reabsorption of phosphorus. A decrease in the alkaline phosphatase staining reaction in the tubules of patients with phosphate diabetes has been reported, but not universally. An unusual anatomical configuration of the renal tubules described as a "swan neck configuration," as well as reduced alkaline phosphatase staining reaction has been reported in the closely related but more complicated renal tubular defect described by Fanconi. Availability of renal punch biopsy should make possible further histochemical study in a variety of renal tubular syndromes.

For a number of years Albright has explained the low serum in organic phosphorus in phosphate diabetes partially on the basis of secondary hyperparathyroidism. It is true that in some of the pathological studies of the parathyroid glands in the disease chief cell hyperplasia has been present. There is no definite proof, however, that this hyperplasia represents a hyperfunctioning state. The stimulus for secondary hyperparathyroidism has been considered to be either a high serum phosphorus or a low serum calcium. In phosphate diabetes the former occurs rarely, and the latter is found infrequently. Even in the infant case of Harrison where serum calcium and phosphorus were followed almost from birth there was no exciting hypocalcemia or hyperphosphatemia that might have acted as an initial stimulus for compensatory hyperparathyroidism.

The normo-phosphaturia in deficiency rickets, where secondary hyperparathyroidism is also thought to be in action is in contrast to the frequently seen increased renal clearance of phosphorus in phosphate diabetes. If functioning secondary hyperparathyroidism is in force in both conditions, the hyperphosphaturia only in phosphate diabetes remains unexplained. This evidence favors a primary renal phosphorous loss as the cause for the hyperphosphaturia in phosphate diabetes rather than secondary hyperparathyroidism.

Withdrawal of phosphorus from the skeleton and osteomalacia would be the natural consequence of an abnormal urinary phosphorus loss unless there was replacement from a dietary source. This concept would designate the disease purely as one of disturbed phosphorus metabolism and would relegate the importance of calcium and vitamin D to a lesser role. If phosphorus is withdrawn from the skeleton due to a negative phosphorus balance, mobilization of skeletal calcium would also occur. This does not appear in the urine since the urinary calcium is depressed in most cases. That this mobilized calcium in phosphate diabetes may be excreted into the intestines, has received support from the report of Swann. This investigator found on balance studies in patients with the disease that calcium excretion in the stools exceeded the intake.

Since the initial interest in phosphate diabetes many pathogenic mechanisms other than those already discussed have been proposed. In 1932 Cockayne, when commenting on the reported cases of resistant rickets, wondered whether these patients were not suffering from an osseous dystrophy determined genetically rather than from acquired rickets. The idea of a basic defect in osteoid tissue, possibly enzymatic in nature causing difficulty in ossification, has since been commented upon by many other authorities on bone metabolism. An even more generalized disturbance of phosphorus metabolism at the cellular level has found some laboratory support. Sterns and Warweg found the organic acid soluble ester phosphorus of the red blood cells to be increased despite the depressed serum inorganic phosphorus. In one case of phosphate diabetes the serum phospho-lipid fraction was increased twofold. An answer
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to the significance of these observations may be found in the more complete analysis
of the various phosphorus containing fractions of the serum and red blood cells
before and after treatment.
That sub-clinical exposure to toxic agents could cause phosphate diabetes is worthy
of consideration. Inhibition of tubular mechanisms is utilized in the action of certain
drugs such as benemid and sodium para-aminohippuric acid. Both of these substances
have been shown to have as one of their actions the reduced renal tubular reabsorption
of phosphorus. In lead poisoning and in Wilson's disease hyperphosphaturia has
been reported, possibly resulting from an inhibition of renal tubular enzyme systems
by excessive concentrations of lead and copper respectively. Of even possible greater
significance is the production in rats by Harrison of excessive excretion of urinary
phosphorus by the injection of maleate. In this instance, glucosuria and amino-aciduria
also occurred. The possibility that in phosphate diabetes some unknown toxic substances
impairing the renal tubular transport mechanisms of phosphorus and causing hyperpho-
sphaturia has not been excluded. The high family incidence might then be explained
on the basis of a common exposure. There is evidence that certain other renal tubular
defects such as idiopathic hypercalcemia results from renal tubular damage due to
pyelonephritis. There is no evidence to support such a mechanism in phosphate diabetes.

SUMMARY
A clinical review of the disease entity, phosphate diabetes, based on the study of
150 cases gathered from the world literature is presented. The postulate that the
entity is due to an intrinsic resistance to vitamin D is critically reviewed. Evidence is
discussed that would preferentially designate the condition to result from a primary
urinary phosphorus loss, followed in turn by hypophosphatemia and osteomalacia.

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Table 1 — Adult Cases of Phosphate Diabetes

<table>
<thead>
<tr>
<th>AGE OF ONSET (YRS)</th>
<th>SEX</th>
<th>AGE AT DIAGNOSIS</th>
<th>PRESENTING SYMPTOMS</th>
<th>LOSS OF HT.</th>
<th>PSEUDO FRACTURES</th>
<th>INITIAL (MG.M.%) CALCIUM</th>
<th>PHOS.</th>
<th>ALK. PHOS.</th>
<th>VITAMIN D PER DAY (MG.M.%)</th>
<th>DURING TREATMENT (MG.M.%) PHOS.</th>
<th>ALK. PHOS.</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>M</td>
<td>19</td>
<td>Pain in tibia. Later in knees and entire skeleton.</td>
<td>+</td>
<td></td>
<td>1.2</td>
<td></td>
<td></td>
<td>Cod Liver Oil</td>
<td>11.0</td>
<td>0.9</td>
<td>Wassermann in CSF positive, in serum negative. Enlarged parathyroids 850 mgm.</td>
</tr>
<tr>
<td>15</td>
<td>F</td>
<td>20</td>
<td>Rolling gait. Bone pain Weakness.</td>
<td>+</td>
<td></td>
<td>10.5</td>
<td>2.5</td>
<td>23</td>
<td>(N3-13) 500,000 IU</td>
<td>10.8</td>
<td>4.5</td>
<td>Parathyroid exploration. Tumor-like degeneration of osteoid tissue moved from right removed from right femur.</td>
</tr>
<tr>
<td>35</td>
<td>F</td>
<td>39</td>
<td>Bone pain. Advancing weakness.</td>
<td>+ +</td>
<td></td>
<td>9.3</td>
<td>1.6</td>
<td>6.68</td>
<td>U. 125,000 IU</td>
<td>8.1</td>
<td>2.5</td>
<td>6.68</td>
</tr>
<tr>
<td>54</td>
<td>M</td>
<td>56</td>
<td>Lower back pain. Later in knees and ankles.</td>
<td>+ +</td>
<td></td>
<td>9.9</td>
<td>1.4</td>
<td>2.2</td>
<td>Bod. 210,000 IU</td>
<td>8.9</td>
<td>1.8</td>
<td>3.3</td>
</tr>
<tr>
<td>57</td>
<td>M</td>
<td>53</td>
<td>Lower back pain. ? Childhood ? 53</td>
<td>+ +</td>
<td></td>
<td>10.2</td>
<td>9.2</td>
<td>1.8</td>
<td>25 KA 600,000 IU</td>
<td>10</td>
<td>3.8</td>
<td>10KA Neurofibromatosis.</td>
</tr>
<tr>
<td>29</td>
<td>M</td>
<td>33</td>
<td>Stiff back. Later pain and muscular weakness in lower extremities.</td>
<td>+ +</td>
<td></td>
<td>10.6</td>
<td>1.9</td>
<td>11.2</td>
<td>Bod. 500,000 IU</td>
<td>14.2</td>
<td>74</td>
<td>CSF albumin increased to 220 mgm.</td>
</tr>
<tr>
<td>AGE OF ONSET</td>
<td>SEX</td>
<td>AGE AT DIAGNOSIS</td>
<td>PRESENTING SYMPTOMS</td>
<td>LOSS OF HT.</td>
<td>PSEUDO FRACTURES</td>
<td>INITIAL (MGM.%) CALCIUM</td>
<td>ALK. PHOS.</td>
<td>VITAMIN D PER DAY</td>
<td>DURING TREATMENT (MGM.%)</td>
<td>ALK. PHOS.</td>
<td>COMMENTS</td>
<td></td>
</tr>
<tr>
<td>-------------</td>
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<td>-----------</td>
<td>-----------------</td>
<td>--------------------------</td>
<td>----------</td>
<td>----------</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>M</td>
<td>24</td>
<td>Backache after a fall. Later pain R. foot and leg.</td>
<td>+</td>
<td>+</td>
<td>11.0</td>
<td>0.9</td>
<td>8 Bod.</td>
<td>100,000 USP</td>
<td>12.8</td>
<td>2.4</td>
<td>History of syphilis</td>
</tr>
<tr>
<td>33</td>
<td>F</td>
<td>52</td>
<td>Bedridden dwarf.</td>
<td>+</td>
<td>+</td>
<td>1.5</td>
<td>0.0</td>
<td>250,000 E</td>
<td>1,000,000 IU</td>
<td>Low</td>
<td>1.5</td>
<td>Neurofibromatosis</td>
</tr>
<tr>
<td>58</td>
<td></td>
<td></td>
<td>Bone pain.</td>
<td>+</td>
<td>+</td>
<td>Norm.</td>
<td>Low</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Neurofibromatosis</td>
</tr>
<tr>
<td>19</td>
<td>F</td>
<td>33</td>
<td>Pain in feet. Increasing weakness. Later generalized bone pain.</td>
<td>+</td>
<td>+</td>
<td>10.6</td>
<td>0.7</td>
<td>over 25 Bod.</td>
<td>200,000 N</td>
<td>2.4</td>
<td>Lowered. (Intermittent minimal glycosuria). Parathyroids showed areas of hyperplasia.</td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>F</td>
<td>35</td>
<td>Bone pain first in back and leg.</td>
<td>+</td>
<td>+</td>
<td>11.0</td>
<td>2.0</td>
<td>6.6 Bod.</td>
<td>100,000 USP</td>
<td>10.0</td>
<td>2.2</td>
<td>4 Parathyroidectomy. Showed some areas of Parathyroid hyperplasia.</td>
</tr>
<tr>
<td>37</td>
<td>M</td>
<td>41</td>
<td>Back pain. Then lawful limbs incapacitated.</td>
<td>+</td>
<td>+</td>
<td>9.1</td>
<td>3.1</td>
<td>8.0 Bod.</td>
<td>(Large dose)</td>
<td>9.6</td>
<td>5.6</td>
<td>1.4 Bod. Neurofibromatosis.</td>
</tr>
</tbody>
</table>