Further Observations on the Arthropathy of Calcium Pyrophosphate Crystal Deposition Disease[1]

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The arthropathy of calcium pyrophosphate dihydrate (CPPD) crystal deposition disease is distinctive and may affect lumbar spinal and sacroiliac joints, as well as appendicular joints. Subchondral pseudocysts that are a hallmark of the disease have a variable appearance, but often occur as a typical cluster of subchondral, coalescent lucencies with smudged, sclerotic margins. Structural joint collapse with fragmentation of cartilage and bone may occur and appear to be related, at least in some cases, to antecedent pseudocysts. Characteristic intra-articular osteochondral bodies are often extensive and may affect multiple joints; their pathogenesis is discussed. Articular synovial calcification is common and may be due to calcium hydroxyapatite, as well as CPPD, particularly if advanced degenerative changes are present. Recognition of the radiologic features that may be encountered in CPPD crystal deposition disease is important for differential diagnosis.

INDEX TERMS: Arthritis • Chondrocalcinosis, 4(0).760 • Joints, diseases • Pseudogout, 4(0).761 • Pyrophosphate

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In 1970 Martel *et al.* recognized that the arthropathy associated with the pseudogout syndrome, or calcium pyrosphosphate dihydrate (CPPD) deposition disease, was a degenerative, but roentgenologically distinctive, disorder (1). It occurred in joints not usually affected by common osteoarthritis, such as the metacarpophalangeal, radiocarpal, tibiotalar, and elbow joints, and was associated with subchondral, cyst-like rarefactions, bone fragmentation, and soft-tissue calcification. It was also observed that the arthropathy could precede radiologically detectable cartilage calcification. These observations have since been confirmed by others (2, 3) and additional features have been noted. Other joints, such as the retropatellar and talonavicular, seem to be selectively affected (3). Destruction of large joints can mimic ischemic necrosis or neuropathic joint disease (4–6), and articular synovial calcification may be marked (7). A similar arthropathy may occur in hemochromatosis (8–10); its occurrence, particularly in the metacarpophalangeal joints, has been regarded as more indicative of the latter diagnosis than "idiopathic chondrocalcinosis" (11). In addition we observed abnormalities of the sacroiliac joints and lumbar spine in two cases, which were associated with discrete subchondral lucencies, similar to those in the appendicular joints.

In view of these reports and our own recent observations, we determined to restudy this condition. Our specific objectives were to (*a*) reevaluate the radiologic features of the associated arthropathy, (*b*) study the nature and pattern of the soft-tissue calcification, (*c*) determine the prevalence and character of sacroiliac and lumbar arthropathy, and (*d*) determine the prevalence of hemochromatosis and its relationship to metacarpophalangeal arthritis in this condition.

MATERIALS AND METHODS

The medical records and roentgenograms of 44 patients, diagnosed as having CPPD deposition disease, were reviewed. Four patients were excluded because they had additional rheumatic diseases; two had psoriatic arthritis, one had rheumatoid arthritis, and another had gout. The remaining 40 cases were included on the basis of the following criteria. Twenty-two had CPPD crystals demonstrated in joint fluid. (A total of 26 patients underwent joint fluid aspirations.) Five additional patients exhibited these crystals in synovial tissue obtained at surgery. The remaining 13 patients were included because they had chondrocalcinosis, typical arthropathy on radiologic examination in one or more joints, and joint effusions that were not otherwise explained. There were 28 men and 12 women, ranging in age from 48 to 91 years, with a mean age of 72.

Thirteen of the 40 patients returned for prospective clinical evaluations. The following laboratory tests were

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TABLE I: APPENDICULAR SKELETAL FEATURES

Feature	No. Cases
Cyst-like lucencies, 1-cm diameter or greater	25
Subchondral collapse	13
Intra-articular osteochondral fragments	21
Distribution of calcification:	
Fibrocartilage	30
Hyaline cartilage	21
Hyaline, not fibrocartilage	0
No chondrocalcinosis	9
Synovial	24
Synovial, no chondrocalcinosis	3
Tendon	7

performed wherever possible in these cases: HLA-B27, latex test for rheumatoid factor, serum iron, iron binding capacity, ferritin, calcium, phosphorus, alkaline phosphatase, bilirubin, serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), and total serum protein. The clinical follow-up period exceeded two years in 21 patients and five years in 15.

Complete radiologic surveys of appendicular joints, lumbar spine, and sacroiliac joints were available in 16 patients. In thirteen of these the examinations were performed as part of this study. These examinations were frequently tailored to evaluate particular features. In this regard, conventional laminograms and computerized tomograms of the spine were obtained in nine and two cases, respectively. The joint surveys were moderately complete in 14 cases and varied in completeness in the remaining 10. The lumbar spine was examined in 28 cases and the sacroiliac joints in 30. The cervical spine was examined in three patients and four underwent roentgenography of the dorsal spine. The interval between the first and last radiologic examination exceeded two years in 20 patients and five years in 10.

Roentgenograms of the lumbar spine and sacroiliac joints of 28 individuals were used as controls. There were various indications for these examinations, including urinary tract disease and possible metastatic neoplasm. These were evaluated for chondrocalcinosis and abnormalities of the disk-vertebral and sacroiliac joints. These patients ranged in age from 54 to 93, with an average age of 72. The ratio of men to women was 2 to 1.

Synovial tissues from seven joints (six knees, one hip), obtained from five patients who underwent joint surgery, were studied histologically and submitted for mineral analysis. Three or more of the following techniques were employed in the mineral analysis of each specimen: chemical, infra-red, emission spectroscopy, and x-ray diffraction.

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Fig. 3. A 50-year-old woman gymnastics teacher with bilateral hip pain.

a. 1971. Multiple coalescent osteolytic areas in both femoral heads (shown on abduction to be mostly subchondral). Note abscence of sclerotic margins, particularly on the right. At this time she had calcification of fibrocartilages of both knees and wrists and typical arthropathy of metacarpophalangeal joints, but no joint effusions.

b. Ten montns later. There is further loss of articular cartilage bilaterally, collapse of the subchondral cortex on the left and, to a lesser extent, the right, regional osteoporosis, and minimal bone apposition of the femoral necks medially. She subsequently underwent total hip arthroplasties; then back pain developed, associated with spinal and sacroiliac involvement (Fig. 16). CPPD crystals in fluid from a knee were first demonstrated several years later, and serum biochemical tests, performed as part of this investigation in 1979, indicated that she had hemochromatosis.

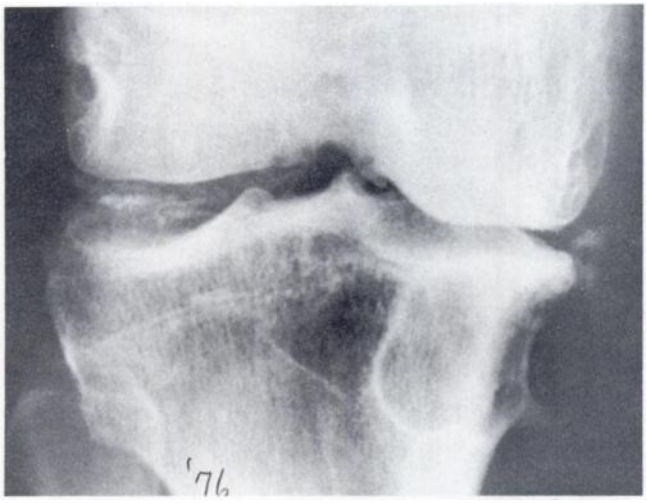


Fig. 1. Discrete, subchondral cyst-like tibial lucency, 2.5 cm in vertical diameter, with sharp, sclerotic margins in a 56-year-old man. Note chondrocalcinosis, narrowing of the cartilage space medially with subchondral sclerosis, and additional lucencies in the lateral femoral condyle and intercondylar notch.

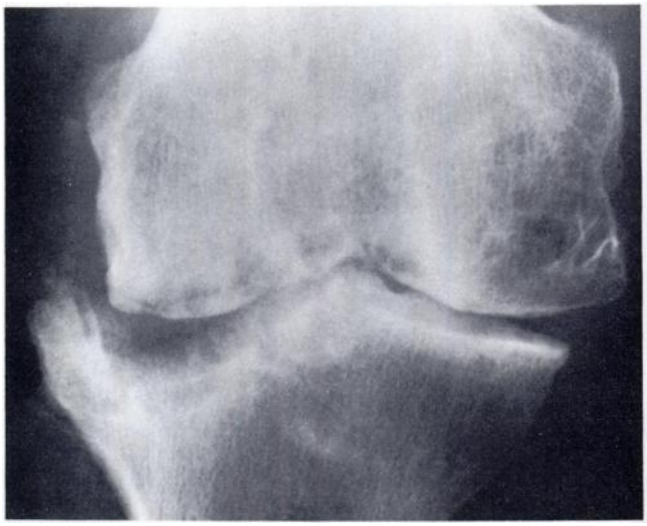
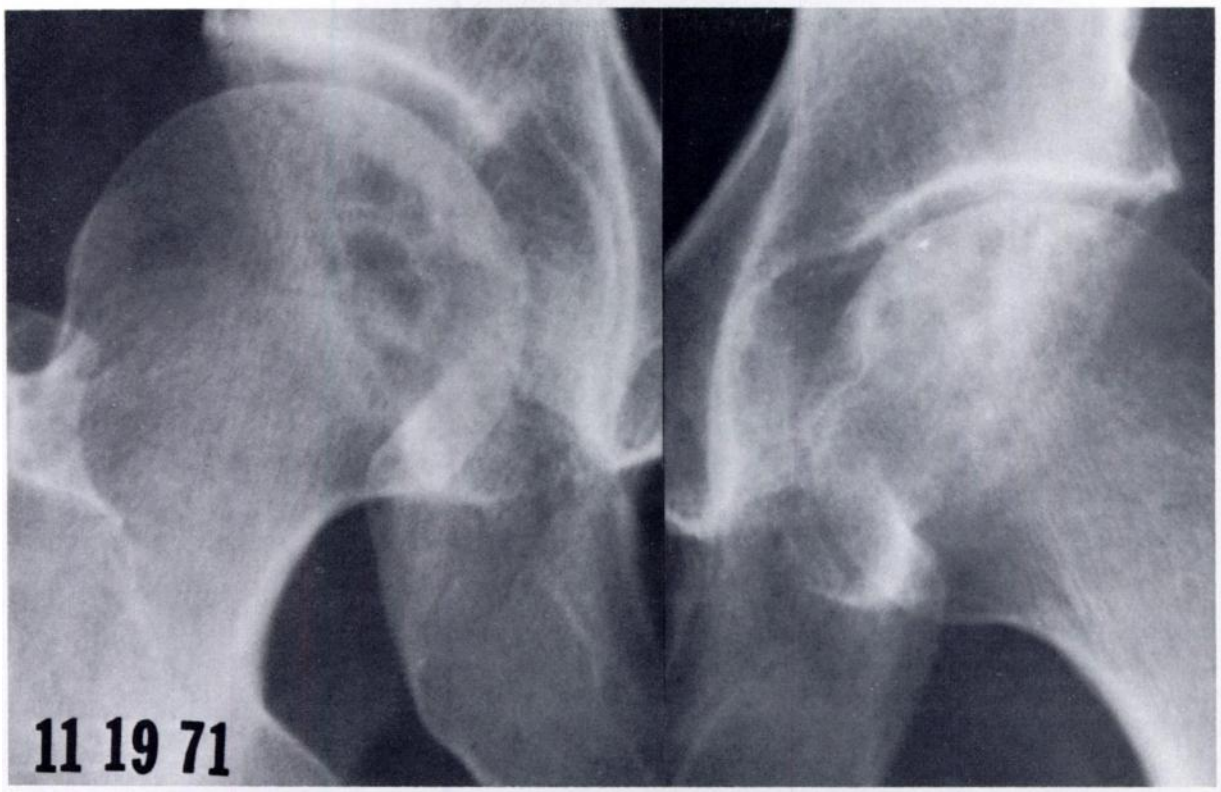


Fig. 2. Man, age 70, with CPPD disease. Multiple, coalescent subchondral lucencies, aligned on distal femoral margin, like a "string of beads," and collapse of lateral tibial plateau with small calcific fragments in adjacent soft tissues. Note degenerative changes medially.



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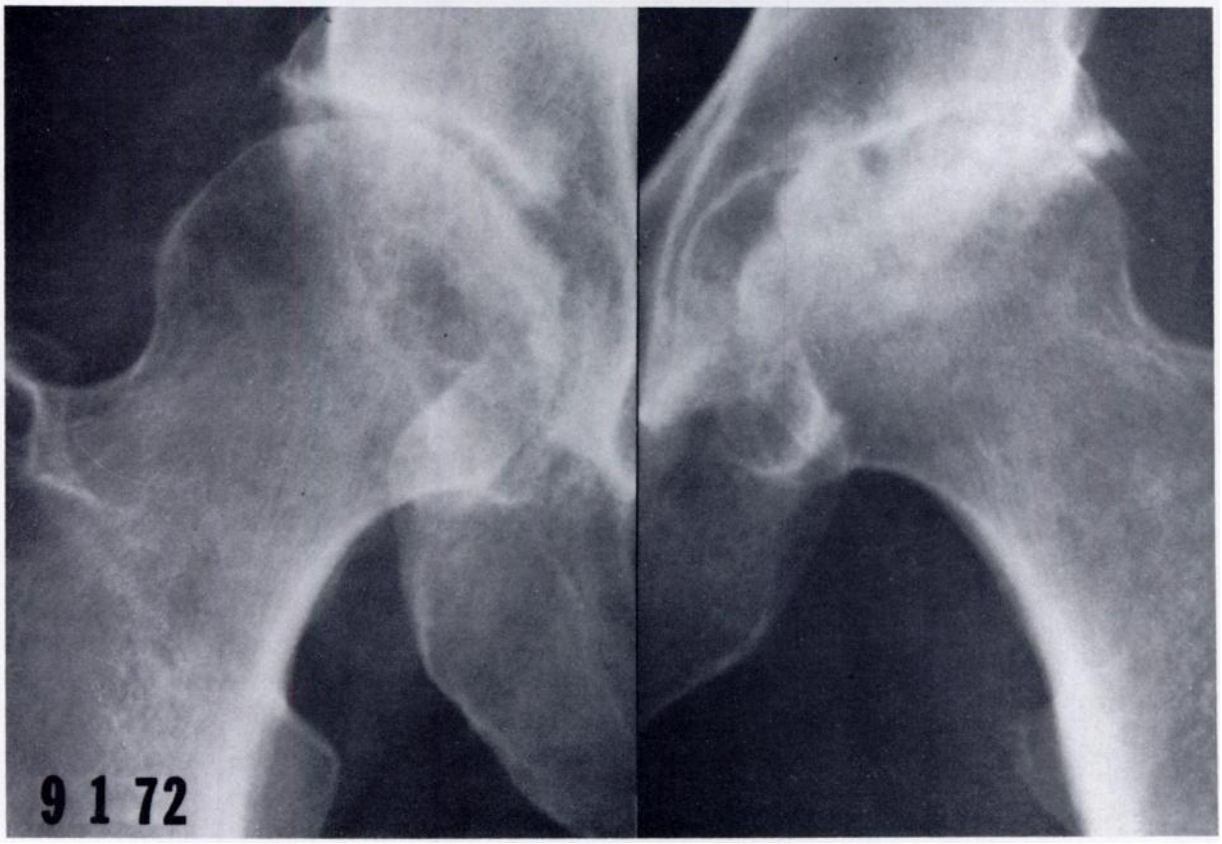

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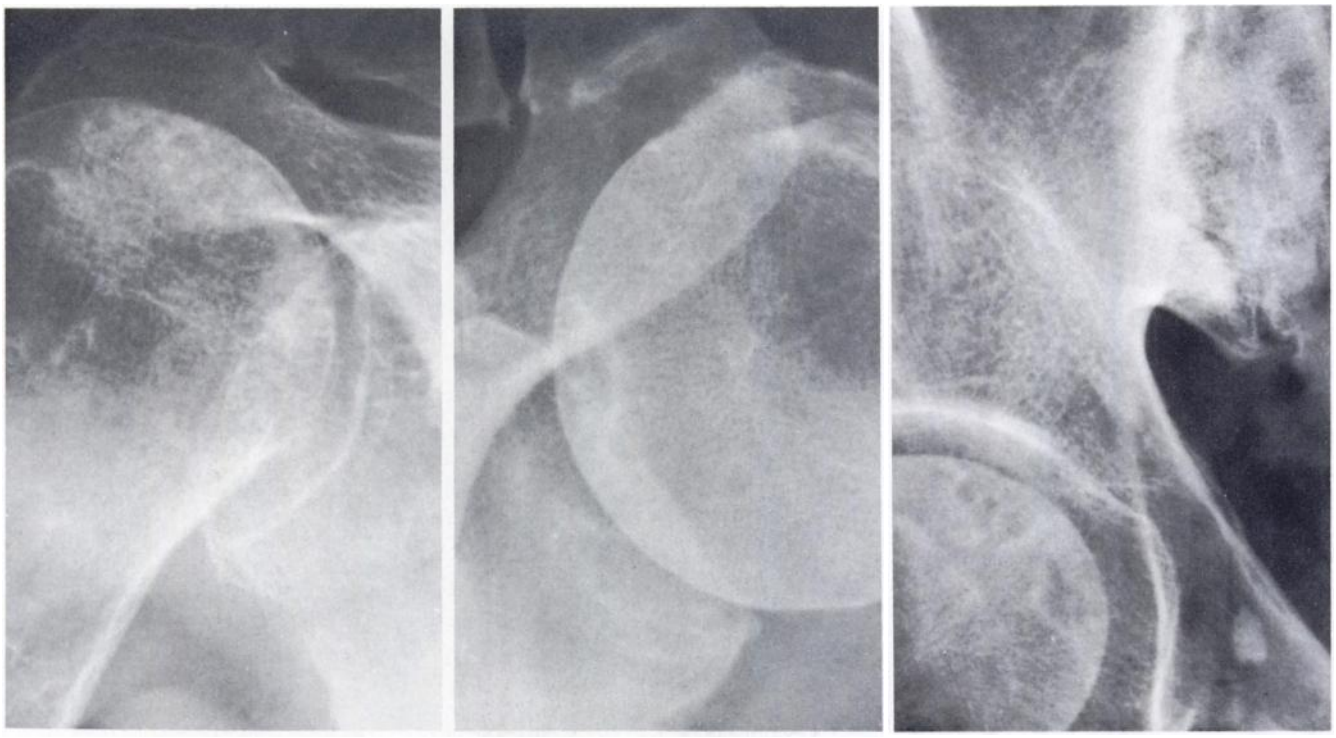


Fig. 4. Distinctive cluster of small coalescent lucencies with smudged, sclerotic borders in two humeri and one femur of three patients. The cartilage spaces are relatively preserved. The patient in (**a**) had hemochromatosis as did probably also the patient in (**b**), but the one in (**c**) had normal serum iron, iron binding capacity, and liver function tests. Figures 3 and 4b are from the same patient, and Figures 4c and 17 are from another.

RESULTS

Clinical Features

Joint effusions were documented on physical examination in 33 cases and there was a history of low back pain in 21. Two of twenty-six patients tested had the rheumatoid factor (latex fixation, titre >1:640), but neither had overt rheumatoid arthritis. Only one of eight patients tested had the HLA-B27 antigen. Of these eight patients, seven had abnormalities of the disk-vertebral joints and five had abnormal sacroiliac joints. The patient with a positive test had bilateral sacroiliac joint erosions, but no clinical or other radiologic evidence of ankylosing spondylitis; this positive test was regarded as coincidental.

Serum iron level was increased in two of 19 patients tested, and the percent saturation of transferrin exceeded the normal (80%) in two of 18 patients. Serum ferritin was elevated in three of 12 patients. These results indicated that, at most, four patients had hemochromatosis, and only in one was the disease clinically overt. This patient had abnormal liver function tests. Nine patients in whom serum indices for hemochromatosis were determined had involvement of the metacarpophalangeal joints; only in two of these were the indices abnormal.

Analyses of synovial tissue for mineral content showed the presence of CPPD and calcium hydroxyapatite in all five patients (seven specimens). The relative quantities of these minerals varied, but the pyrophosphate was 10–25 times more plentiful by weight than the hydroxyapatite. In addition, carbonate apatite was present in four specimens.

Radiologic and Pathologic Features

Appendicular Joints: The significant findings in the appendicular joints are summarized in TABLE I. Discrete cyst-like lucencies, or cavities (geodes), 1 cm or greater in diameter, were noted in 25 patients (Fig. 1). Similar, smaller cavities were common. These cavities were virtually always subchondral and often appeared coalescent or aligned like a "string of beads" on the subchondral margin (Fig. 2). Although they usually had sclerotic borders, which varied from being sharply defined to indistinct, some cases exhibited no sclerotic margins (Fig. 3). They often had a distinctive appearance as a cluster of small coalescent lesions with smudged, sclerotic borders (Fig. 4).

Collapse of an articular surface with varying degrees of bone fragmentation was present in 13 cases. This was most frequent in the knee and hip (Figs. 2 and 3). At times the appearance resembled a neuropathic joint or advanced ischemic necrosis (Figs. 5 and 6). In two cases the collapse could be related to preexisting subchondral cavities (Fig. 3).

Osteochondral intra-articular fragments, present in 21

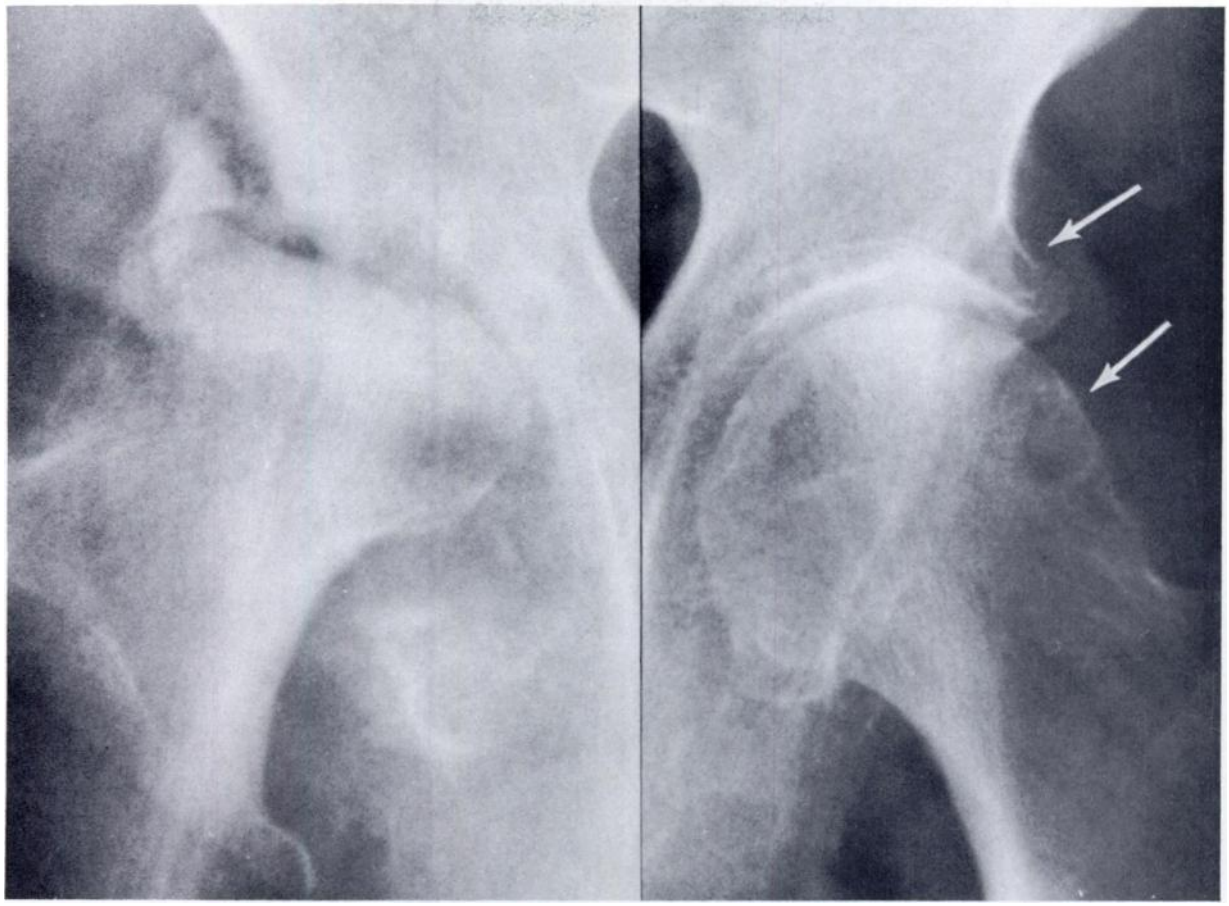


Fig. 5. Woman, age 71, with advanced arthropathy of CPPD disease. There is a collapse of the femoral head and fragmentation, simulating neuropathic joint disease. Note discrete lucencies in left femoral head and contiguous acetabulum (arrows) with very little narrowing of cartilage space.

cases, were always accompanied by degenerative articular changes, which were usually severe. The joints most commonly affected were the knee and elbow (Fig. 7). More than one joint was affected in seven cases, and in two of these the calcified bodies increased in size and number over several years. In several cases, these osteochondral bodies were remarkably extensive, particularly in the knee (Fig. 8).

Calcification occurred in both fibrocartilage and hyaline cartilage. It was most common in the former and in no case did it occur in the latter alone. Chondrocalcinosis was not evident in nine cases, but in six of these the joint surveys were incomplete. (However, the knee and wrists were included in two of the six cases.)

Synovial intra-articular calcification having characteristically fluffy, poorly defined contours was suspected in 24 cases. Joints most often affected were the knee, shoulder, wrist, and metacarpophalangeal (Figs. 9 and 10). At times it was difficult to distinguish such calcification from osteochondral fragments when both were present (Fig. 11). If a distinct cortex was evident, it was interpreted as osteochondral fragment, but an amorphous appearance suggested synovial calcification. Occasionally, calcification had an irregular "popcorn"-like configuration, typical of calcification in cartilage. It was recognized that all types of calcification could be present simultaneously (Fig. 11). Synovial calcification was present in three patients who did not have chondrocalcinosis, but in two of these the joint surveys were incomplete. In the third case the calcification was minimal and present only in a knee.

Seven patients exhibited tendon calcifications. The most frequently affected tendons were the Achilles, triceps, and gastrocnemius. An interesting observation was that the calcification often extended far from the tendon attachment (Fig. 12).

Crystalline deposits were identified histologically in thickened, fibrotic synovium from the knee or hip of five patients. In routinely-stained hematoxylin and eosin preparations, the deposits appeared as circumscribed aggregates of blue-grey or purple material. When examined with polarized light, a multitude of small rectangular, rhomboid, and rod-shaped birefringent crystals, characteristic of CPPD, became easily visible. The concentration of crystals varied considerably among patients, and also in different areas of synovium from the same patient. Some

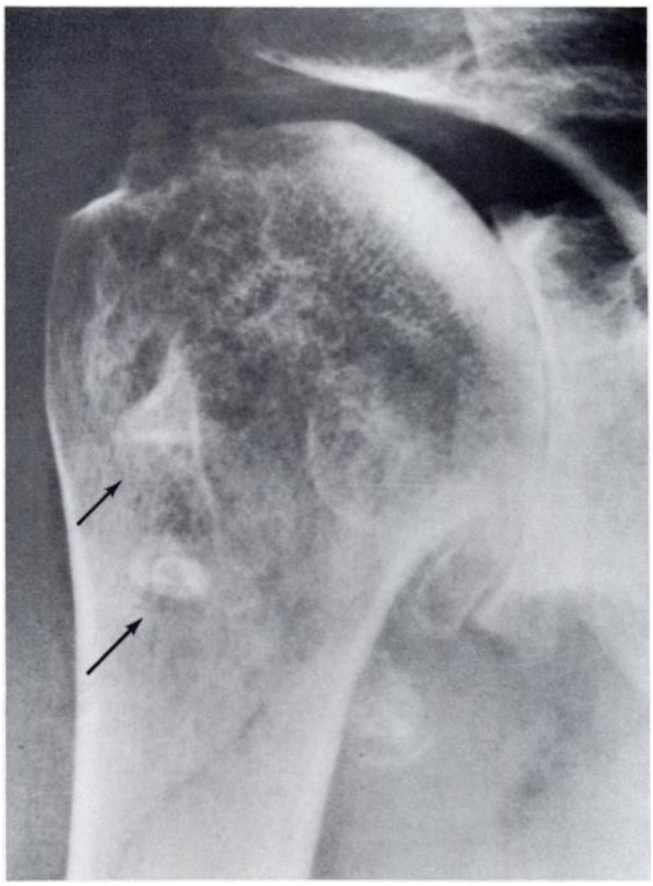


Fig. 6. Advanced arthropathy of CPPD disease resembling neuropathic joint disease or advanced ischemic necrosis. There is virtually complete loss of articular cartilage with multiple, small lucencies aligned along the sclerotic, humeral margin. Note osteochondral fragments, inferomedially and projected over the humerus (arrows). The other shoulder was similarly affected.

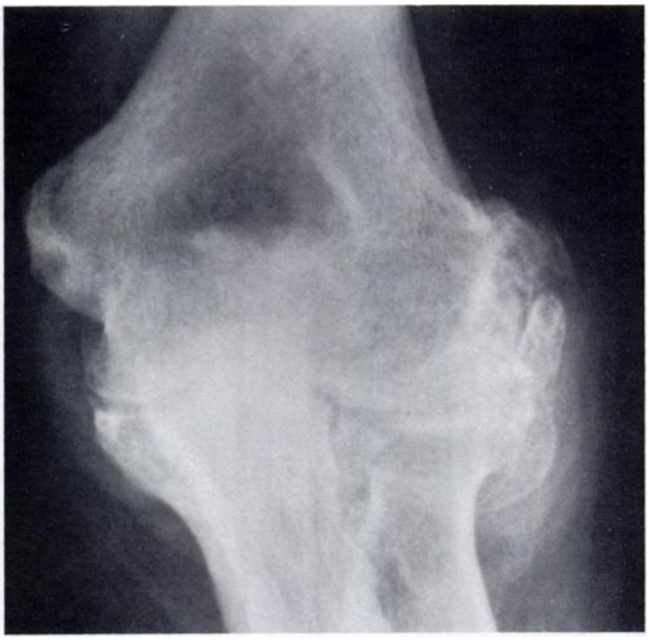


Fig. 7. Intra-articular osteochondral fragments in CPPD disease. The other elbow was similarly affected.

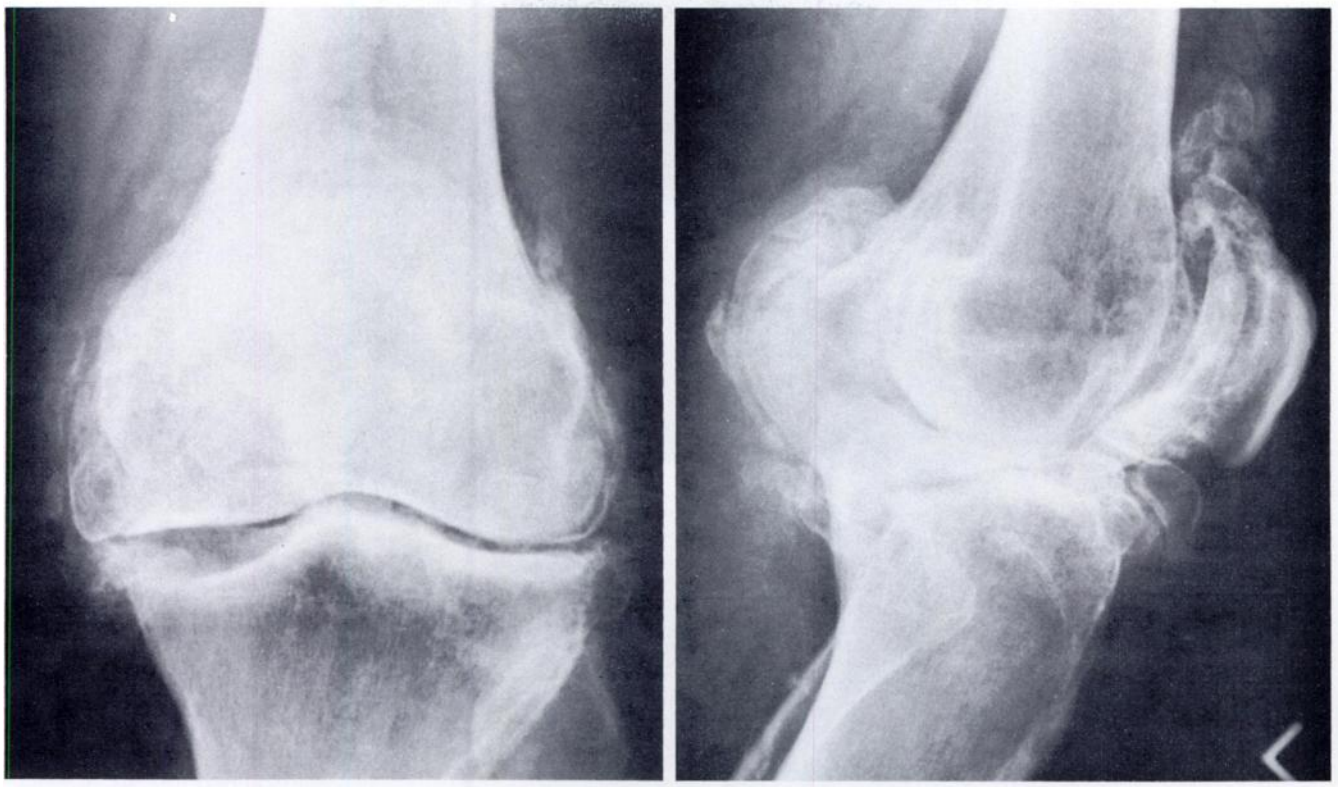
deposits were surrounded by an inflammatory cellular infiltrate consisting predominantly of macrophages and synovial lining cells. In some instances, a foreign body giant cell reaction was also seen. Many of the deposits, however, were embedded in dense fibrous tissue and were unaccompanied by any cellular inflammatory reaction. Crystalline deposits were also occasionally seen within articular cartilage and fibrocartilage. Small foci of probable chondroid metaplasia of the synovium were identified in two patients; osteochondromatous loose bodies were present in one of these cases and in another patient.

The resected pieces of articular bone were involved by degenerative changes, similar to those seen in osteoarthritis. Subchondral pseudocysts of various sizes were present in some specimens. They consisted of discrete rounded spaces surrounded by fibrous and granulation tissue and were devoid of an epithelial lining.

The prevalence of radiologically typical arthropathy in various appendicular joints is listed in TABLE II. For the purpose of this study, "typical arthropathy" was defined as a degenerative process (loss of articular cartilage, subchondral sclerosis, and a varying degree of osteophyte formation) associated with any of the following features: (*a*) discrete subchondral rarefactions, (*b*) collapse of the subchondral cortex with bone fragmentation, (*c*) articular osteochondral bodies, (*d*) involvement of a joint not generally affected by common osteoarthritis. In the case with metatarsophalangeal arthritis there was bilateral involvement of multiple joints, including the metacarpophalangeal (Fig. 13). Eight patients had chondrocalcinosis of the symphysis pubis and one had severe erosive changes with a vacuum phenomenon in this joint. This patient had bilateral sacroiliac joint erosions as well.

Spine: The lumbar spine and sacroiliac joints were commonly affected (TABLE III). The lumbar spine was evaluated in 28 cases. Seven patients had lumbar disk annulus calcification at multiple levels. Disk narrowing secondary to degenerative disease, as indicated by subchondral sclerosis and osteophyte formation, was noted at one level in six cases and at two or more levels in nine. The degenerative changes in these cases were often severe (Fig. 14). A vacuum disk phenomenon was observed at one level in six cases and at two or more levels in nine (Fig. 15). Degenerative changes were usually present at the affected levels. Moderate to severe osteoarthritis of the apophyseal joints was present in 11 cases and often associated with mild spondylolisthesis. In one case it was characterized by multiple, coalescent subchondral lucencies, documented by laminograms and computerized tomography (Fig. 16). These lucencies were similar to those in the appendicular joints.

Sacroiliac joint abnormalities were detected in 14 of 30 patients evaluated. Subchondral erosions, evident in six cases, were diffuse and bilateral in three. Reactive scle-



8a,b

Fig. 8. Remarkably extensive osteochondral bodies in left knee of 69-year-old man with CPPD disease. The other knee was similarly affected. The appearance could be confused with neuropathic joint disease.
a. Frontal view.
b. Lateral view.

rosis was present in two of the latter, simulating ankylosing spondylitis (Fig. 17). The erosions were multifocal in two cases (Fig. 16 d and e) and in one there was a solitary, unilateral erosion (Fig. 18). A vacuum phenomenon was observed in both sacroiliac joints in seven cases (Fig. 14b) and in one case it was unilateral.

None of the control cases had disk annulus calcification. Although degenerative disk disease and vacuum phenomenon were frequent at one level, such lesions were relatively uncommon at two or more levels, compared with the CPPD cases. Sacroiliac joint erosions were not observed and only one patient exhibited a vacuum phenomenon in one sacroiliac joint. These differences were statistically significant ($p < .05$) for disk calcification, vacuum disk at two or more levels, sacroiliac erosions, and sacroiliac vacuum phenomenon. The difference in incidence of degenerative disk disease at two or more levels is of questionable significance ($p < .30$), but the fact that the difference for vacuum disk phenomenon at two or more levels was significant may in part reflect the greater severity of the disk changes in the disease subjects.

DISCUSSION

Zitnan and Sitaj were the first to recognize the condition now called calcium pyrophosphate dihydrate (CPPD) deposition disease as a distinct clinical entity (12,13). Shortly thereafter, Revault *et al.* cited 35 cases, previously reported under various names, and added six of their own (14). McCarty *et al.* emphasized the significance of CPPD crystals in synovial fluid and stressed the importance of radiologic recognition of calcification in the joint cartilages (15). The role of radiology became more significant when it was realized that the arthropathy had distinctive radiologic features, aside from the chondrocalcinosis (1), and that this could be an important clue to the diagnosis, particularly when chondrocalcinosis is not evident (3).

The subchondral pseudocysts are one of the hallmarks of this arthropathy. In retrospect, it is of interest that they were present in three of the six cases first reported by McCarty *et al.* (15). Although they appear to be nonspecific histologically and no different from those in common osteoarthritis, they frequently have distinctive radiologic features. They are typically multiple and commonly occur in more than a single joint. They are usually subchondral, but vary in size and shape. The largest one in our series was 2.5 cm in greatest diameter (Fig. 1). In most cases there is a sclerotic margin, although its sharpness varies. A distinctive appearance, not usually observed in ordinary osteoarthritis, is a cluster of coalescent lucencies with slightly sclerotic, smudged, indistinct margins (Figs. 3 and 4) or a zoning of multiple small contiguous lucencies along

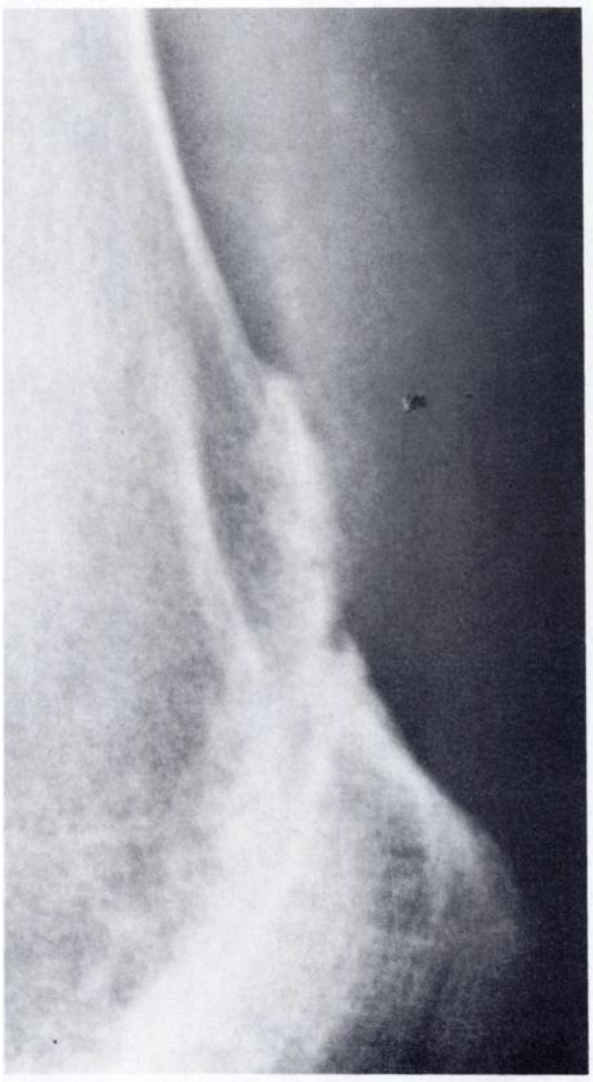


Fig. 9. Amorphous calcification in fluid-containing suprapatellar bursa of knee in CPPD disease. This appearance was interpreted as synovial calcification.

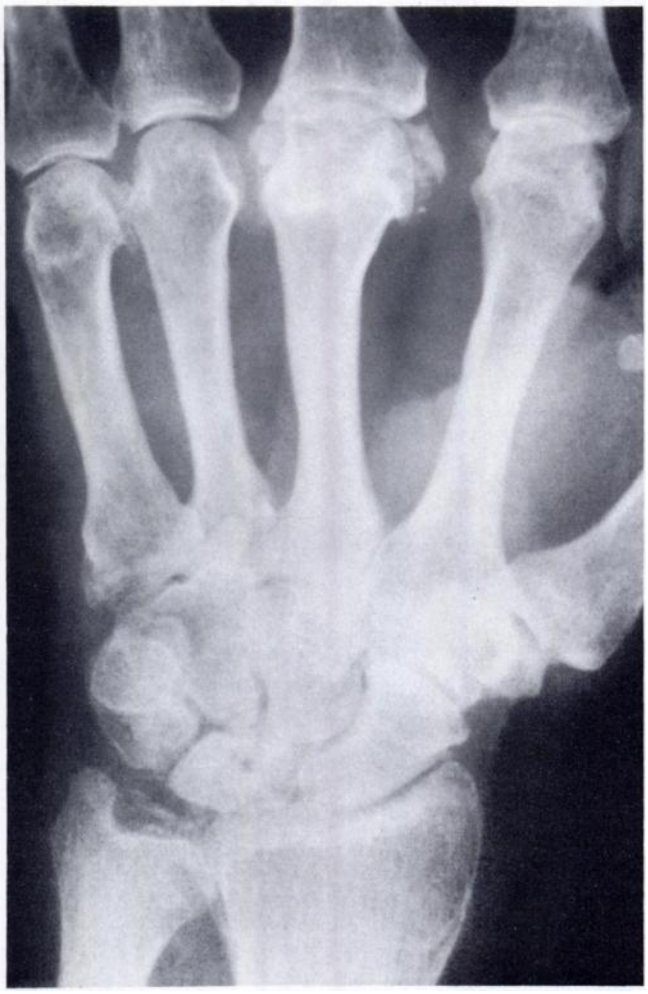
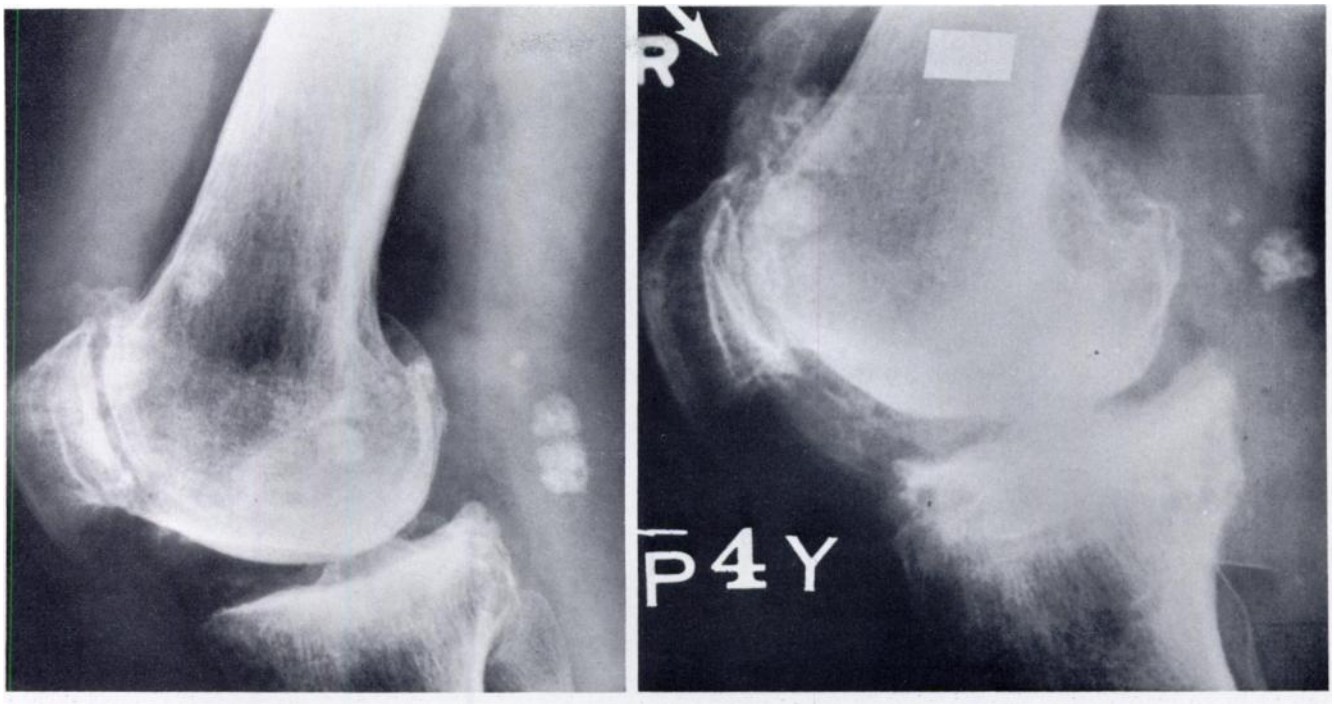


Fig. 10. Amorphous calcification in metacarpophalangeal joint of middle finger interpreted as within synovium. Note chondrocalcinosis in wrist, loss of radiocarpal cartilage space, and lytic areas in lunate and navicular.

the subchondral border. Such configurations may be important clues to the diagnosis. In addition, in several cases the lucencies were present prior to significant loss in thickness of the articular cartilage, sclerosis of the subchondral cortex, or osteophyte formation. Although a large subchondral pseudocyst may rarely precede other changes in common osteoarthritis, particularly in the hip, this feature may also be a clue to this arthropathy, particularly if the accompanying pseudocysts have this distinctive appearance.

Severe destructive arthropathy of large joints is not an uncommon manifestation. Its association with bone fragmentation and pseudocysts suggests that the latter may be important in its pathogenesis. We have postulated that the latter cause weakening of bone structure such that mechanical stress of everyday usage leads to collapse of the subchondral bone. Although the development of the arthropathy is typically insidious, the fact that severe destruction can occur within months (Fig. 3) supports this interpretation. The radiologic appearance can easily be confused with neuropathic joints or ischemic necrosis, particularly if there is rapid progression. Although CPPD crystals have been described in patients with neuropathic joints (16), the relationship may be coincidental (17). It is significant that none of our cases had clinical evidence of neuropathic bone disease or clinical or histologic evidence of ischemic necrosis. In our experience such destructive arthropathy is more apt to be "pseudoneuropathic" (17). Radiologists should consider CPPD disease in the differential diagnosis of rapidly progressive destruction of large joints.

The proliferation of numerous osteochondral bodies is a characteristic and fascinating feature, the pathogenesis of which is not entirely clear. It may originate as chondral or osteochondral fracture fragments that receive nourishment from the synovium and increase in size. Endo-



11a,b

Fig. 11. a. A 60-year-old man with CPPD disease, exhibiting joint effusion, degenerative changes, and multiple intra-articular calcifications that have an irregular, "popcorn-like," but sharply marginated, configuration, suggesting calcification in cartilaginous bodies.
b. Four years later. There is a remarkable increase in calcification, particularly at the anterosuperior (arrow) and anteroinferior aspects. Osteochondral fragments and extensive synovial calcification were found at surgery. In this case it is difficult in retrospect to distinguish these radiologically.

chondral bone formation may occur if such fragments obtain a blood supply by attaching to the synovial tissue. Osteochondral bodies are commonly associated with degenerative joint disease. In this situation "shredding" of articular surfaces presumably releases small chondral fragments that can undergo hyperplasia and likewise attach to the synovium. Both initiating mechanisms may be operative in CPPD; subchondral fragmentation is known to occur and degenerative disease is characteristic. However, the profuseness of these osteochondral bodies and the fact that multiple joints are often affected makes this a remarkable feature. Conceivably, chronic hyperemia, associated with inflammation and CPPD deposition in the soft tissues, exaggerates this hyperplastic process. The possibility that synovial chondroid metaplasia may be a factor is intriguing, but speculative. In the two cases with such changes the metaplastic foci were minimal and of uncertain significance. Nevertheless, the possibility that such metaplasia could be a factor deserves additional study.

The frequency of synovial calcification in this condition not been widely appreciated. In some cases it is so extensive as to appear to fill the joint cavity. In one report two patients came to needless surgery because extensive knee calcification was confused with synovial osteochondromatosis (7). In addition, we would emphasize that osteochondral fragments and synovial calcification may coexist. The observation that tendons were often calcified over long segments, far beyond their attachments, may be significant. To our knowledge, this has not been noted previously, but its specificity needs to be evaluated.

In this age of total joint arthroplasty, the pathologist may be the first to establish the diagnosis of CPPD deposition disease. The crystalline deposits of CPPD may easily be overlooked during routine microscopic examination of tissues resected from osteoarthritic joints when the deposits are small and few. The pathologist should be constantly alerted to their possible presence and should be familiar with their histologic features. The crystalline deposits are most easily seen in the synovial and associated articular soft tissues, where they tend to be concentrated in circumscribed nests near the edges. Deposits within articular cartilage are less frequently found, especially when there has been extensive destruction of the hyaline cartilage. When the deposits are large and numerous, they must be distinguished from the crystalline deposits of gout. The use of polarized microscopy is essential in identifying these crystals and differentiating them from urate crystals in tissues. Small rectangular, rhomboid, and rod-shaped birefringent crystals are more characteristic of CPPD than urate. The latter typically consist of long, needle-shaped crystals. Furthermore, fixation in absolute alcohol is not required for the preservation of CPPD. In contrast to the urate crystals of gout, which are water-soluble, they easily withstand aqueous fixatives such as formalin.

The concept of an arthropathy induced by calcium hy-

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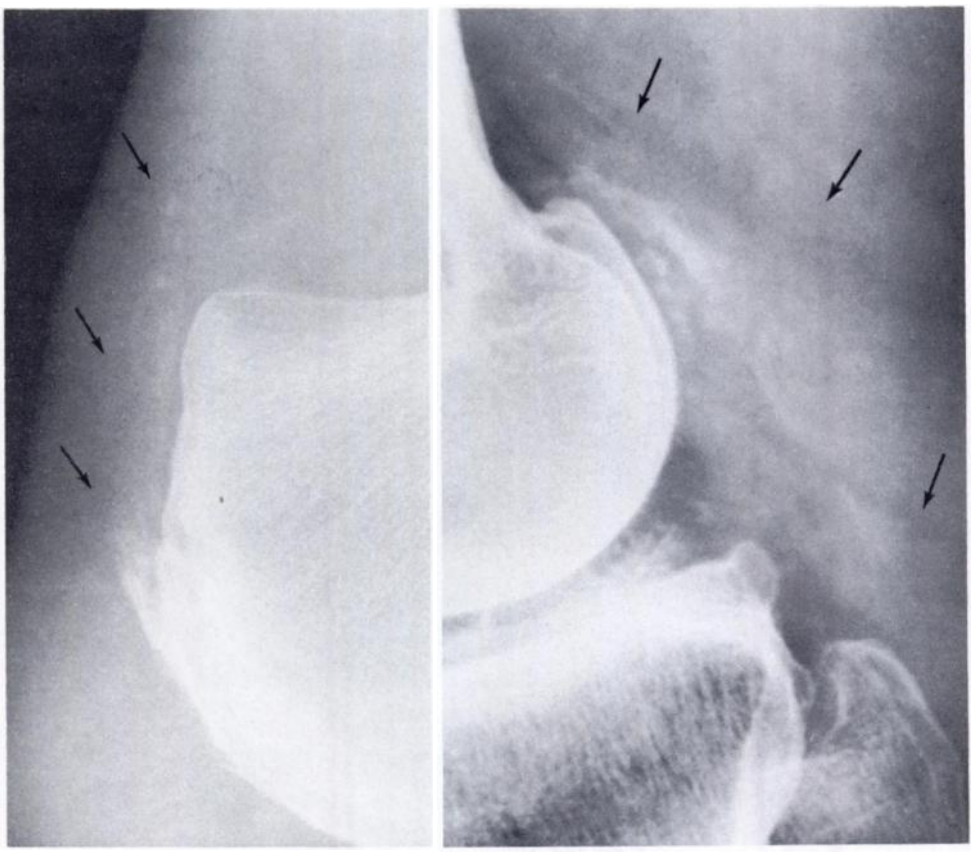

Fig. 12. Multiple tendon calcifications in 64-year-old woman with CPPD disease. Note the length of calcific deposits (arrows).
a. Achilles.
b. Gastrocneumius. Note meniscal calcification.

droxyapatite crystals evolved following the recognition that such crystals could be detected in joint fluid and tissues by high-resolution scanning electron microscopy (18, 19). Although one can reliably differentiate CPPD from urate crystals in fluid with compensated polarized light microscopy, hydroxyapatite crystals are too small to be identified and are not birefringent. According to Schumacher *et al.* (19), with light microscopy purple-staining cytoplasmic inclusions or extracellular globules may suggest the presence of these crystals, but clumps of apatite crystals occasionally mimic urate or CPPD. Nevertheless, using sophisticated analytic techniques, it was soon recognized that hydroxyapatite crystals often coexist in the same joint with CPPD (20). It is of interest that mineral analysis in our five cases showed both types of crystals in synovial tissue. It is important to note that severe osteoarthritis was present in all of these joints. Recent

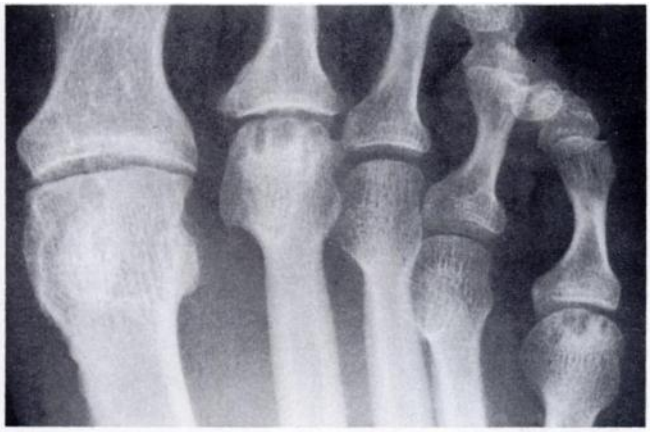

Fig. 13. Typical arthropathy of metatarsophalangeal joints. The other foot was similarly affected and the metacarpophalangeal joints were also selectively involved.

TABLE II: DISTRIBUTION OF CPPD ARTHROPATHY

Joint	No. Cases
Metacarpophalangeal	22
Wrist	19
Knee	18
Hip	12
Elbow	10
Shoulder	7
Ankle	3
Metatarsophalangeal	1
Symphysis pubis	3

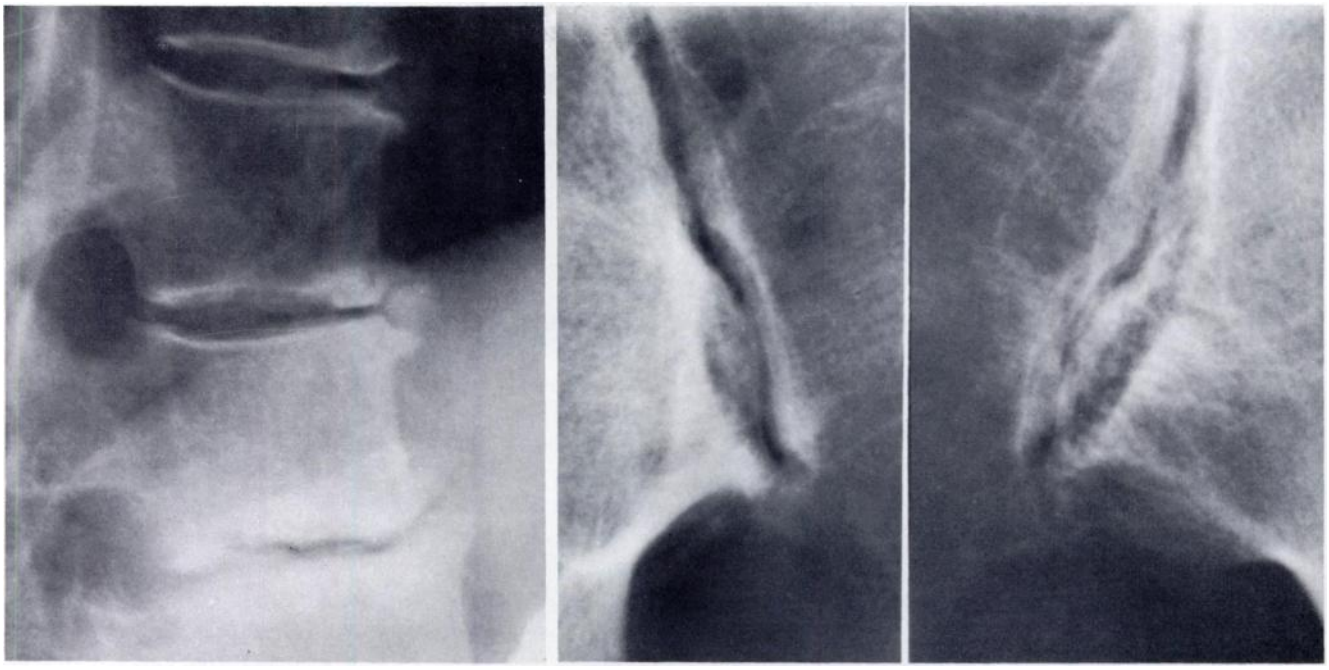

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Fig. 14. Lumbar and sacroiliac joint involvement in 75-year-old woman with CPPD disease.
a. Lumbar disk-vertebral joints. Note disk calcification and vacuum phenomena.
b. Bilateral vacuum phenomena in sacroiliac joints. Note discontinuity of subchondral iliac cortex on left and adjacent alteration in trabecular pattern.

studies have shown that hydroxyapatite crystals may be found intra-articularly, with or without CPPD, in a variety of diseases, particularly in severe osteoarthritis (21, 22). Although it is recognized that hydroxyapatite crystals are capable of inducing joint inflammation, their relationship to the arthropathy is unclear. It is conceivable that joint destruction from different causes, if severe enough, and given the proper biochemical conditions, may itself induce the local release of such crystals from the eroded bone surface, cartilage, or some other source (19, 21, 22). Such causes include ordinary osteoarthritis and pyrophosphate. The finding of both kinds of crystals in patients regarded as having CPPD deposition disease does not necessarily imply that this disease is not a distinct entity.

Back pain is a common complaint among patients with CPPD disease. Although there have been occasional references to spinal arthropathy, other than intervertebral disk calcification (23–26) the prevalence and radiologic features of such arthropathy have not been recognized. Spinal involvement has been known to mimic ankylosing spondylitis clinically (27, 28), but this condition is usually easily differentiated radiologically. Bony ankylosis, squaring of vertebral bodies, and syndesmophyte formation are absent in CPPD disease. Sacroiliac arthropathy does occur in the

TABLE III: LUMBAR DISK-VERTEBRAL AND SACROILIAC JOINTS

Finding	Incidence Arthropathy Subjects	Incidence Controls	Incidence Difference	Significance by Fisher's Exact Test
Lumbar Spine	$N = 28$	$N = 28$		
Disk annulus calcification	7(.25)	0(0)	.25	$p < .005$
Degenerative disk disease:				
1 level	7(.25)	6(.21)	.04	1.0 (n.s.)
2 or more levels	9(.32)	6(.21)	.11	$p < .30$
Vacuum disk phenomenon:				
1 level	6(.21)	5(.18)	.04	1.0 (n.s.)
2 or more levels	9(.32)	2(.07)	.25	$p < .02$
Sacroiliac Joints	$N = 30$	$N = 28$		
Subchondral erosions	6(.20)	0(0)	.20	$p < .015$
Vacuum phenomenon	8(.27)	1(.03)	.24	$p < .02$

n.s. = not significant

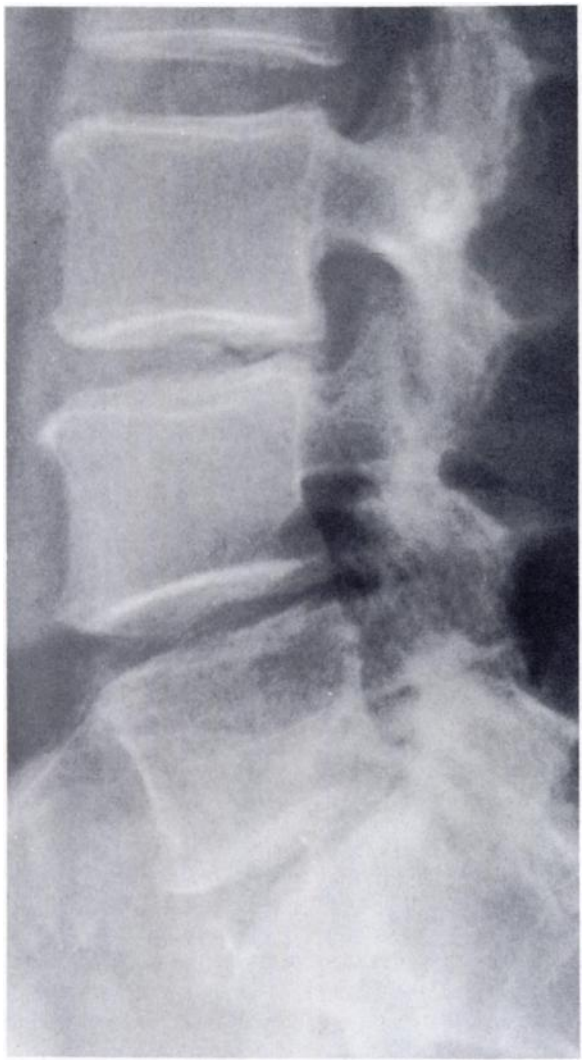

Fig. 15. Calcification, degeneration, and vacuum phenomena in disk-vertebral joints in 65-year-old man with CPPD disease. There is a minimal vacuum effect in disk at L2-3 with calcification, but no disk narrowing.

latter, but only occasionally does it simulate the radiologic appearance of ankylosing spondylitis (Fig. 17). In such cases the patient's age, clinical history, and absence of other radiologic features of ankylosing spondylitis will be helpful.

We recognize that most of our patients were old enough to have ordinary degenerative disease of the spine, unrelated to CPPD disease. However, the severity of the lesions, their association with subchondral cyst-like lucencies in the apophyseal and sacroiliac joints (resembling the lesions in the appendicular joints), and involvement of multiple disk-vertebral levels, particularly with vacuum phenomena, suggest that many of our cases are in a special category. A sacroiliac joint vacuum phenomenon, indicating cartilage degeneration, is nonspecific, but its frequency in these patients compared with controls is significant. Sacroiliac involvement with subchondral cyst formation has recently been noted in familial chondrocalcinosis (28).

The symphysis pubis, composed of fibrocartilage, is structurally similar to the disk-vertebral joints, possibly explaining why similar destructive changes may occur in both. Moderate degenerative changes in the symphysis pubis are common in older individuals, but severe erosive changes are unusual. Such erosive arthritis was observed in only one of our cases, but others have also observed it (3).

The arthropathy of hemochromatosis is radiologically identical to that of CPPD disease. It was not until after Schumacher's description of hemochromatosis arthropathy (8) that patients with hemochromatosis were recognized as often having CPPD disease as well. It is of interest in retrospect that one of the two patients described by Schumacher had calcification of a knee meniscus. Inasmuch as chondrocalcinosis is frequently present in hemochromatosis, the pathogenesis of the arthropathy of hemochromatosis may be identical to that of CPPD disease. Our findings emphasize that this arthropathy is not specific for hemochromatosis and involvement of the metacarpophalangeal joints is not more indicative of hemochromatosis than idiopathic CPPD disease.

It should be recognized that the arthopathy can be present in the absence of chondrocalcinosis. The latter may not be sufficiently dense to be visualized by routine radiologic technique, or severe cartilage destruction may preclude its identification. Furthermore, it is occasionally exhibited by patients who do not give a history of painful joint effusion (pseudogout syndrome). Such a case is illustrated in Figures 3 and 16; in this patient joint effusions first developed years after the arthropathy in her hips was detected.

Recognition of the various radiologic features here described is particularly important for differential diagnosis. Conditions that may be confused with this disease include synovial osteochondromatosis, neuropathic joint disease, ischemic necrosis, ochronosis, and diseases associated with sacroiliac arthritis (29). Inasmuch as the arthropathy is primarily a degenerative process, it can be viewed as simply a severe form of common osteoarthritis. However, the unusual tendency to form pseudocysts, often prior to cartilage narrowing, the predilection for joints not commonly affected by osteoarthritis, its occurrence as a familial disease, and its association with conditions such as hyperparathyroidism and hemochromatosis (30) support the view that the pathogenesis of this condition probably differs from osteoarthritis and that it should, at least for the present, be considered a separate entity.

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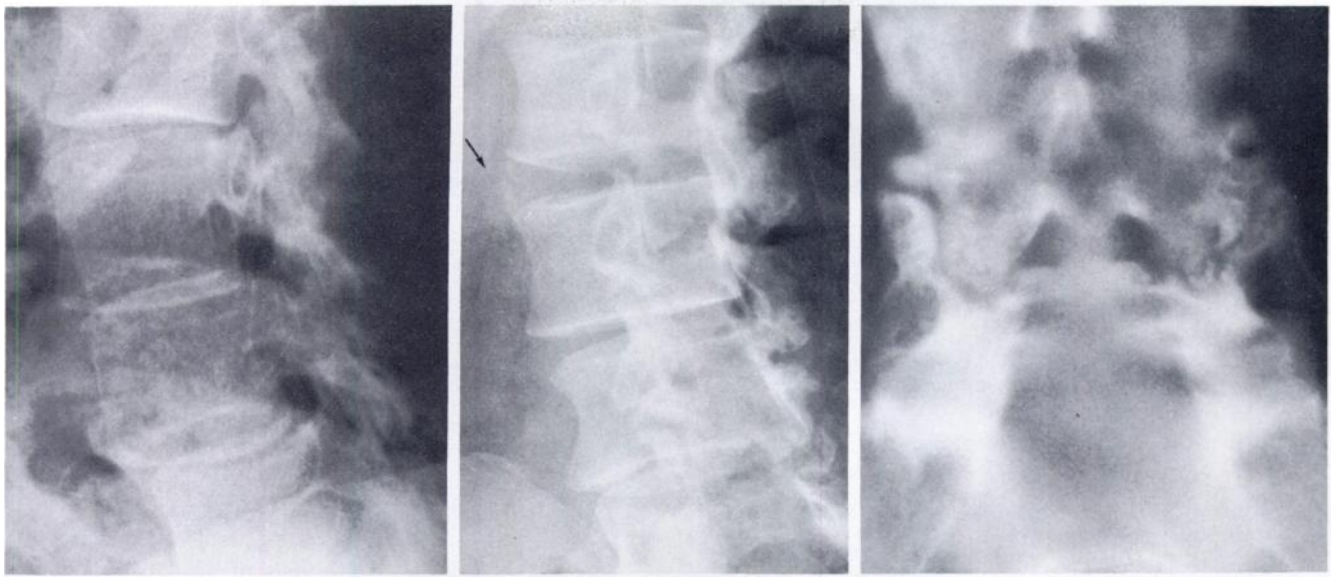

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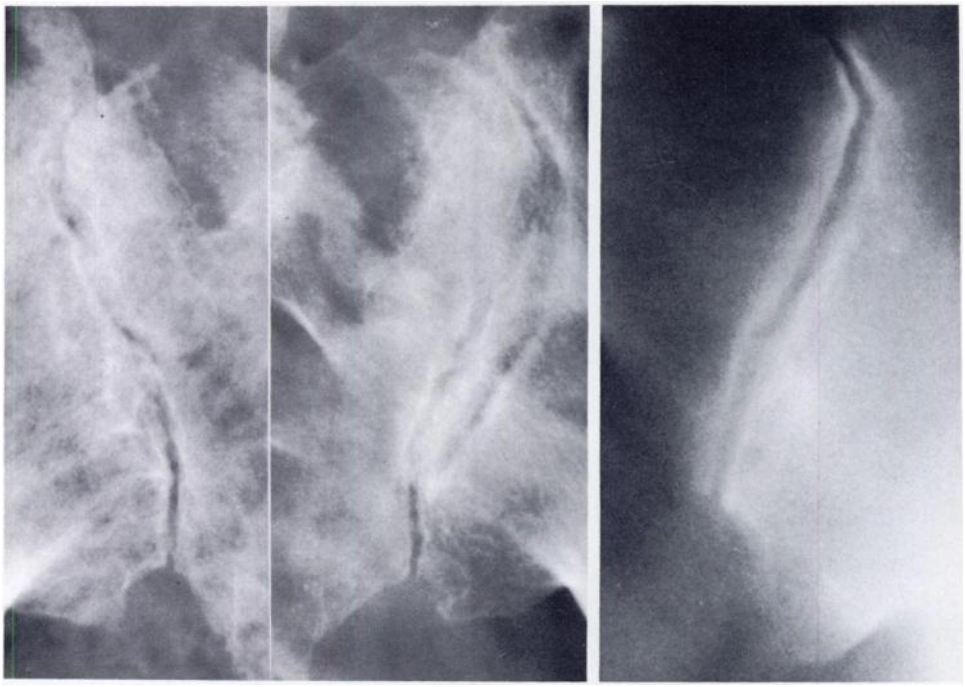

Fig. 16. Spine and sacroiliac joints in the same case as shown in Figure 3. 1979.

a. Moderate spondylolisthesis at L3-4 and L4-5, associated with degenerative disease of apophyseal joints.

b. Oblique view showing disk calcification (arrow) and arthritis of the apophyseal joints.

c. Anteroposterior laminograms of L4-5 apophyseal joints confirming the degenerative changes and showing subchondral, coalescent lucencies analogous to lesions in appendicular joints.

d. Sacroiliac joints, showing subtle erosions of the subchondral cortices with adjacent ill-defined areas of lucency, particularly on the right, and slight reactive sclerosis on the left.

e. Laminagram, left sacroiliac joint, confirming these erosions with adjacent reactive sclerosis. Similar changes were evident on laminagrams of the right sacroiliac joint.

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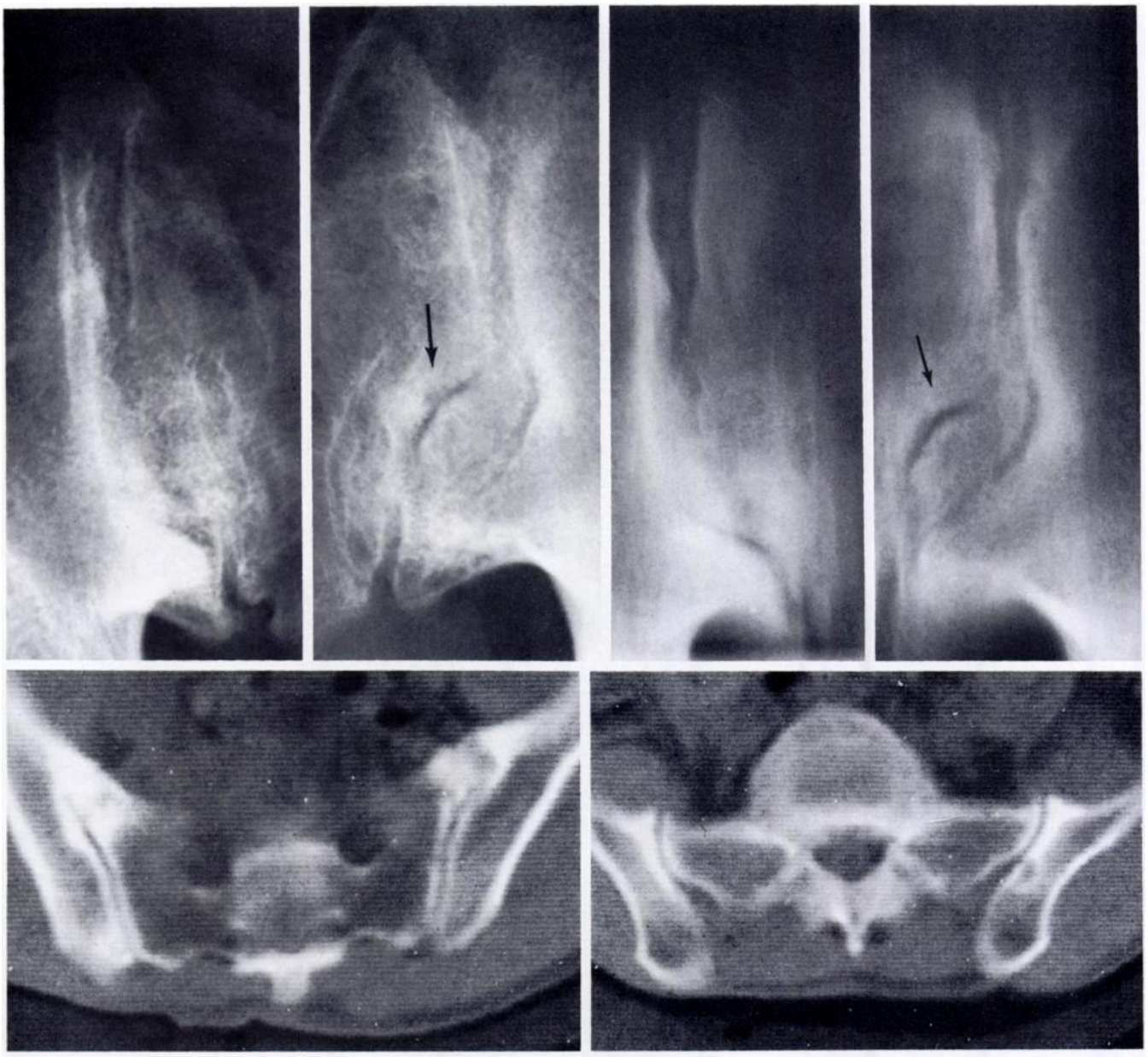

Fig. 17. Sacroiliac joint erosions in 60-year-old man who had low back pain of recent onset and was subsequently shown to have CPPD disease. Same case as in Figure 4c. Although this patient had the B-27 antigen, there was no clinical or radiologic evidence of Reiter disease, psoriatic arthritis, or ankylosing spondylitis.

a. Bone erosions and reactive sclerosis in both sacroiliac joints. Note vacuum phenomenon on left (arrow).
b. Laminagrams confirming sacroiliac abnormalities. Vacuum phenomenon (arrow).
c. CT scan of caudal portions of joints confirming these erosions and sclerosis, particularly anteriorly.
d. More cranial CT section showing subcortical pseudocyst on left.

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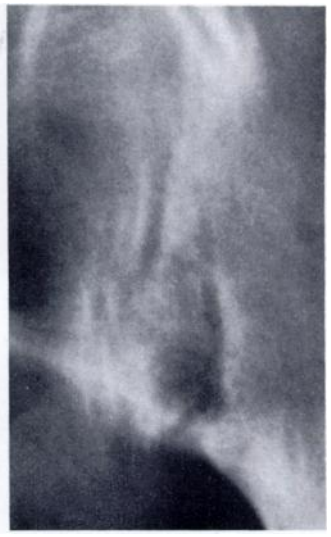

Fig. 18. Unilateral sacroiliac arthropathy in 72-year-old man with CPPD disease. There is an extensive erosion at the antero-inferior aspect of the left sacroiliac joint involving both sacral and iliac margins.