

327 Gout and Other Crystal-Associated Arthropathies

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The use of polarizing light microscopy during synovial fluid analysis in 1961 by McCarty and Hollander and the subsequent application of other crystallographic techniques, such as electron microscopy, energy-dispersive elemental analysis, and x-ray diffraction, have allowed investigators to identify the roles of different microcrystals, including monosodium urate (MSU), calcium pyrophosphate dihydrate (CPPD), calcium apatite (apatite), and calcium oxalate (CaOx), in inducing acute or chronic arthritis or peri-arthritis. The clinical events that result from deposition of MSU, CPPD, apatite, and CaOx have many similarities but also important differences. Prior to the use of crystallographic techniques in rheumatology, much of what was considered to be gouty arthritis in fact was not. Because of often similar clinical presentations, the need to perform synovial fluid analysis to distinguish the type of crystal involved must be emphasized. Polarized light microscopy alone can identify most typical crystals; apatite, however, is an exception. Aspiration and analysis of effusions are also important to assess the possibility of infection. Apart from the identification of specific microcrystalline materials or organisms, synovial fluid characteristics in crystal-associated diseases are nonspecific, and synovial fluid can be inflammatory or noninflammatory. A list of possible musculoskeletal manifestations of crystal-associated arthritis is shown in [Table 327-1](#).

GOUT

Gout is a metabolic disease most often affecting middle-aged to elderly men and postmenopausal women. It is the result of an increased body pool of urate with hyperuricemia. It is typically characterized by episodic acute and chronic arthritis, due to deposition of MSU crystals in joints and connective tissue tophi, and the risk for deposition in kidney interstitium or uric acid nephrolithiasis (Chap. 353).

ACUTE AND CHRONIC ARTHRITIS

Acute arthritis is the most frequent early clinical manifestation of gout. Usually, only one joint is affected initially, but polyarticular acute gout can occur in subsequent episodes. The metatarsophalangeal joint of the first toe is often involved, but tarsal joints, ankles, and knees are also commonly affected. Especially in elderly patients or in advanced disease, finger joints may be involved. Inflamed Heberden's or Bouchard's nodes may be a first manifestation of gouty arthritis. The first episode of acute gouty arthritis frequently begins at night with dramatic joint pain and swelling. Joints rapidly become warm, red, and tender, with a clinical appearance that often mimics cellulitis. Early attacks tend to subside spontaneously within 3–10 days, and most patients have intervals of varying length with no residual symptoms until the next episode. Several events may precipitate acute gouty arthritis: dietary excess, trauma, surgery, excessive ethanol ingestion, hypouricemic therapy, and serious medical illnesses such as myocardial infarction and stroke.

After many acute mono- or oligoarticular attacks, a proportion of gouty patients may present with a chronic nonsymmetric synovitis, causing potential confusion with rheumatoid arthritis (Chap. 314).

TABLE 327-1 MUSCULOSKELETAL MANIFESTATIONS OF CRYSTAL-INDUCED ARTHRITIS

Acute mono- or polyarthritis	Destructive arthropathies
Bursitis	Pseudo-rheumatoid arthritis
Tendinitis	Pseudo-ankylosing spondylitis
Enthesitis	Spinal stenosis
Tophaceous deposits	Crown dens syndrome
Peculiar type of osteoarthritis	Carpal tunnel syndrome
Synovial osteochondromatosis	Tendon rupture

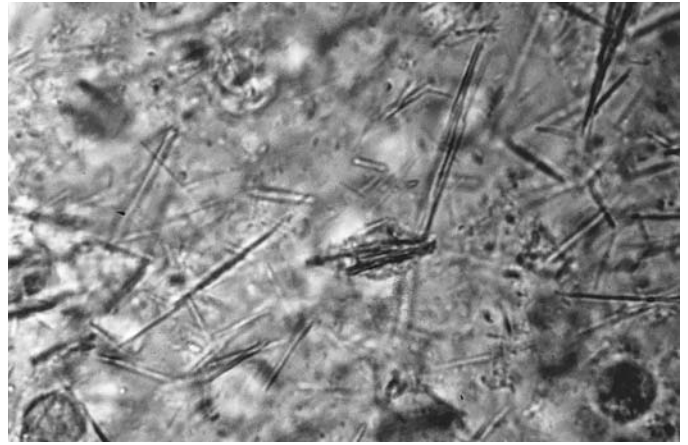


FIGURE 327-1 Extracellular and intracellular monosodium urate crystals, as seen in a fresh preparation of synovial fluid, illustrate needle- and rod-shaped strongly negative birefringent crystals (compensated polarized light microscopy; 400x).

Less commonly, chronic gouty arthritis will be the only manifestation and, more rarely, the disease will manifest only as periarticular tophaceous deposits in the absence of synovitis. Women represent only 5–20% of all patients with gout. Premenopausal gout is rare; it is seen mostly in individuals with a strong family history of gout. Kindreds of precocious gout in young females caused by decreased renal urate clearance and renal insufficiency have been described. Most women with gouty arthritis are postmenopausal and elderly, have osteoarthritis and arterial hypertension causing mild renal insufficiency, and are usually receiving diuretics.

Laboratory Diagnosis Even if the clinical appearance strongly suggests gout, the diagnosis should be confirmed by needle aspiration of acutely or chronically involved joints or tophaceous deposits. Acute septic arthritis, several of the other crystalline-associated arthropathies, palindromic rheumatism, and psoriatic arthritis may present with similar clinical features. During acute gouty attacks, strongly birefringent needle-shaped MSU crystals with negative elongation are typically seen both intracellularly and extracellularly ([Fig. 327-1](#)). Synovial fluid cell counts are elevated from 2000 to 60,000/ μ L. Effusions appear cloudy due to the increased numbers of leukocytes. Large amounts of crystals occasionally produce a thick pasty or chalky joint fluid. Bacterial infection can coexist with urate crystals in synovial fluid; if there is any suspicion of septic arthritis, joint fluid must also be cultured.

MSU crystals can also often be demonstrated in the first metatarsophalangeal joint and in knees not acutely involved with gout. Arthrocentesis of these joints is a useful technique to establish the diagnosis of gout between attacks.

Serum uric acid levels can be normal or low at the time of the acute attack, as inflammatory cytokines can be uricosuric and effective initiation of hypouricemic therapy can precipitate attacks. This limits the value of serum uric acid determinations for the diagnosis of gout. Nevertheless, serum urate levels are almost always elevated at some time and are important to use to follow the course of hypouricemic therapy. A 24-h urine collection for uric acid can, in some cases, be useful in assessing the risk of stones, in elucidating overproduction or underexcretion of uric acid, and in deciding if it might be appropriate to use a uricosuric therapy (Chap. 353). Excretion of >800 mg of uric acid per 24 h on a regular diet suggests that causes of overproduction of uric acid should be considered. Urinalysis, serum creatinine, hemoglobin, white blood cell (WBC) count, liver function tests, and serum lipids should be obtained because of possible pathologic sequelae of gout and other associated diseases requiring treatment, and as baseline because of possible adverse effects of gout treatment.

Radiographic Features Early in the disease radiographic studies may only confirm clinically evident swelling. Cystic changes, well-defined

327-2 erosions with sclerotic margins (often with overhanging bony edges), and soft tissue masses are characteristic radiographic features of advanced chronic tophaceous gout.

Rx GOUT

ACUTE GOUTY ARTHRITIS The mainstay of treatment during an acute attack is the administration of anti-inflammatory drugs such as non-steroidal anti-inflammatory drugs (NSAIDs), colchicine, or glucocorticoids. NSAIDs are most often used in individuals without complicating comorbid conditions. Both colchicine and NSAIDs may be poorly tolerated and dangerous in the elderly and in the presence of renal insufficiency and gastrointestinal disorders. In attacks involving one or two joints, intraarticular glucocorticoid injections may be preferable and effective. Ice pack applications and rest of the involved joints can be helpful. Colchicine given orally is a traditional and effective treatment, if used early in the attack. One to two 0.6-mg tablets can be given every 6–8 h over several days with subsequent tapering. This is generally better tolerated than the formerly advised hourly regimen. The drug must be stopped promptly at the first sign of loose stools, and symptomatic treatment must be given for the diarrhea. Intravenous colchicine is occasionally used, e.g., as pre- or postoperative prophylaxis in 1- to 2-mg doses when patients cannot take medications orally. Life-threatening colchicine toxicity and sudden death have been described with the administration of >4 mg/d IV. The IV colchicine should be given slowly through an established venous line over 10 min in a soluset. The total dose should never exceed 4 mg.

NSAIDs given in full anti-inflammatory doses are effective in ~90% of patients, and the resolution of signs and symptoms usually occurs in 5–8 days. The most effective drugs are any of those with a short half-life and include indomethacin, 25–50 mg tid; ibuprofen, 800 mg tid; or diclofenac, 50 mg tid. Oral glucocorticoids such as prednisone, 30–50 mg/d as the initial dose and gradually tapered with the resolution of the attack can be effective in polyarticular gout. For single or few involved joints intraarticular triamcinolone acetonide, 20–40 mg, or methylprednisolone, 25–50 mg, have been effective and well tolerated. Adrenocorticotropic hormone (ACTH) as an intramuscular injection of 40–80 IU in a single dose or every 12 h for 1–2 days can be effective in patients with acute polyarticular refractory gout or in those with a contraindication for using colchicine or NSAIDs.

HYPOURICEMIC THERAPY Ultimate control of gout requires correction of the basic underlying defect, the hyperuricemia. Attempts to normalize serum uric acid to <300–360 $\mu\text{mol/L}$ (5.0–6.0 mg/dL) to prevent recurrent gouty attacks and eliminate tophaceous deposits entail a commitment to long-term hypouricemic regimens and medications that generally are required for life. Hypouricemic therapy should be considered when, as in most patients, the hyperuricemia cannot be corrected by simple means (control of body weight, low-purine diet, increase in liquid intake, limitation of ethanol use, and avoidance of diuretics). The decision to initiate hypouricemic therapy is usually made taking into consideration the number of acute attacks (urate lowering may be cost effective after two attacks), serum uric acid levels [progression is more rapid in patients with serum uric acid >535 $\mu\text{mol/L}$ (>9.0 mg/dL)], patient's willingness to commit to lifelong therapy, or presence of uric acid stones. Urate-lowering therapy should be initiated in any patient who already has tophi or chronic gouty arthritis. Uricosuric agents, such as probenecid, can be used in patients with good renal function who underexcrete uric acid, with <600 mg in a 24-h urine sample. Urine volume must be maintained by ingestion of 1500 mL of water every day. Probenecid can be started at a dosage of 250 mg twice daily and increased gradually as needed up to 3 g in order to maintain a serum uric acid level <300 $\mu\text{mol/L}$ (5 mg/dL). Probenecid is generally not effective in patients with serum creatinine levels of >177 $\mu\text{mol/L}$ (2.0 mg/dL). These patients may require allopurinol or benzbromarone (not available in the United States). The latter is another uricosuric drug that is more effective in patients with renal failure. Recent reports have identified that losartan, fenofibrate, and amlodipine have some mild uricosuric effects.

The xanthine oxidase inhibitor allopurinol is by far the most commonly used hypouricemic agent and is the best drug to lower serum urate in overproducers, urate stone formers, and patients with renal disease. It can be given in a single morning dose, 100–300 mg initially and increasing up to 800 mg if needed. In patients with chronic renal disease, the initial allopurinol dosage should be lower and adjusted depending on the serum creatinine concentration; for example, with a creatinine clearance of 10

mL/min, one would generally use 100 mg every other day. Doses can gradually be increased to reach the target urate level; however, more studies are needed to provide exact guidance. Patients with frequent acute attacks may also require lower initial doses to prevent exacerbations. Toxicity of allopurinol has been recognized increasingly in patients with renal failure who use thiazide diuretics and in those patients allergic to penicillin and ampicillin. The most serious side effects include skin rash with progression to life-threatening toxic epidermal necrolysis, systemic vasculitis, bone marrow suppression, granulomatous hepatitis, and renal failure. Patients with mild cutaneous reactions to allopurinol can reconsider the use of a uricosuric agent or undergo an attempt at desensitization to allopurinol. They can also pay increased attention to diet and should be aware of new alternative agents under investigation (see below). Urate-lowering drugs are generally not initiated during acute attacks but after the patient is stable and low-dose colchicine has been initiated to decrease the risk of flares that often occur with urate lowering. Colchicine prophylaxis in doses of 0.6 mg one to two times daily is usually continued, along with the hypouricemic therapy, until the patient is normouricemic and without gouty attacks for 6 months or as long as tophi are present. New urate-lowering drugs undergoing investigation include a PEGylated uricase and a new specific xanthine oxidase inhibitor, febuxostat.

CPPD DEPOSITION DISEASE

PATHOGENESIS

The deposition of CPPD crystals in articular tissues is most common in the elderly, occurring in 10–15% of persons aged 65–75 years and 30–50% of those >85 years. In most cases this process is asymptomatic, and the cause of CPPD deposition is uncertain. Because >80% of patients are >60 years and 70% have preexisting joint damage from other conditions, it is likely that biochemical changes in aging or diseased cartilage favor crystal nucleation. In patients with CPPD arthritis there is an increased production of inorganic pyrophosphate and decreased levels of pyrophosphatases in cartilage extracts. Mutations in the *ANKH* gene described in both familial and sporadic cases can increase elaboration and extracellular transport of pyrophosphate. The increase in pyrophosphate production appears to be related to enhanced activity of ATP pyrophosphohydrolase and 5'-nucleotidase, which catalyze the reaction of ATP to adenosine and pyrophosphate. This pyrophosphate could combine with calcium to form CPPD crystals in matrix vesicles or on collagen fibers. There are decreased levels of cartilage glycosaminoglycans that normally inhibit and regulate crystal nucleation. In vitro studies have demonstrated that transforming growth factor β_1 and epidermal growth factor both stimulate the production of pyrophosphate by articular cartilage and thus may contribute to the deposition of CPPD crystals.

Release of CPPD crystals into the joint space is followed by the phagocytosis of these crystals by monocyte-macrophages and neutrophils, which respond by releasing chemotactic and inflammatory substances.

A minority of patients with CPPD arthropathy have metabolic abnormalities or hereditary CPPD disease (Table 327-2). These associations suggest that a variety of different metabolic products may enhance CPPD deposition either by directly altering cartilage or inhibiting inorganic pyrophosphatases. Included among these conditions are hyperparathyroidism, hemochromatosis, hypophosphatasia, and hypomagnesemia. The presence of CPPD arthritis in individuals <50 years old should lead to consideration of these metabolic disorders and inherited forms of disease, including those identified in a variety of ethnic groups (Table 327-2). Genomic DNA studies performed on different kindreds have shown a possible location of genetic defects on chromosome 8q or on chromosome 5p in a region that expresses the gene of the membrane pyrophosphate channel (*ANKH* gene). Mutations as noted above described in the *ANKH* gene in kindreds with CPPD arthritis can increase extracellular pyrophosphate and induce CPPD crystal formation. Investigation of younger patients with CPPD deposition should include inquiry for evidence of familial aggregation and evaluation of serum calcium, phosphorus, alkaline phosphatase, magnesium, serum iron, and transferrin.

TABLE 327-2 CONDITIONS ASSOCIATED WITH CALCIUM PYROPHOSPHATE DIHYDRATE DISEASE

Aging
Disease-associated
Primary hyperparathyroidism
Hemochromatosis
Hypophosphatasia
Hypomagnesemia
Chronic gout
Postmeniscectomy
Epiphyseal dysplasias
Hereditary: Slovakian-Hungarian, Spanish, Spanish-American (Argentinian, ^a Colombian, and Chilean), French, ^a Swedish, Dutch, Canadian, Mexican-American, Italian-American, ^a German-American, Japanese, Tunisian, Jewish, English ^a

^aMutations in the *ANKK1* gene.

CLINICAL MANIFESTATIONS

CPPD arthropathy may be asymptomatic, acute, subacute, or chronic or cause acute synovitis superimposed on chronically involved joints. Acute CPPD arthritis was originally termed *pseudogout* by McCarty and coworkers because of its striking similarity to gout. Other clinical manifestations of CPPD deposition include (1) induction or enhancement of peculiar forms of osteoarthritis; (2) induction of severe destructive disease that may radiographically mimic neuropathic arthritis; (3) production of symmetric proliferative synovitis, clinically similar to rheumatoid arthritis and frequently seen in familial forms with early onset; (4) intervertebral disk and ligament calcification with restriction of spine mobility, mimicking ankylosing spondylitis (also seen in hereditary forms); and (5) rarely spinal stenosis (most commonly seen in the elderly) (Table 327-1).

The knee is the joint most frequently affected in CPPD arthropathy. Other sites include the wrist, shoulder, ankle, elbow, and hands. Rarely, the temporomandibular joint and ligamentum flavum of the spinal canal are involved. Clinical and radiographic evidence indicates that CPPD deposition is polyarticular in at least two-thirds of patients. When the clinical picture resembles that of slowly progressive osteoarthritis, diagnosis may be difficult. Joint distribution may provide important clues suggesting CPPD disease. For example, primary osteoarthritis rarely involves a metacarpophalangeal, wrist, elbow, shoulder, or ankle joint. If radiographs reveal punctate and/or linear radiodense deposits in fibrocartilaginous joint menisci or articular hyaline cartilage (*chondrocalcinosis*), the diagnostic likelihood of CPPD disease is further enhanced. *Definitive diagnosis* requires demonstration of typical crystals in synovial fluid or articular tissue (Fig. 327-2). In the absence of joint effusion or indications to obtain a synovial biopsy, chondrocalcinosis is presumptive of CPPD deposition. One exception is chondrocalcinosis due to CaOx in some patients with chronic renal failure.

Acute attacks of CPPD arthritis may be precipitated by trauma. Rapid diminution of serum calcium concentration, as may occur in severe medical illness or after surgery (especially parathyroidectomy), can also lead to pseudogout attacks.

In as many as 50% of cases, episodes of CPPD-induced inflammation are associated with low-grade fever and, on occasion, temperatures as high as 40°C. Whether or not radiographic proof of chondrocalcinosis is evident in the involved joint(s), synovial fluid analysis with microbial cultures is essential to rule out the possibility of infection. In fact, infection in a joint with any microcrystalline deposition process can lead to crystal shedding and subsequent synovitis from both crystals and microorganisms. Synovial fluid in acute CPPD disease has inflammatory characteristics. The leukocyte count can range from several thousand cells to 100,000 cells/μL, the mean being about 24,000 cells/μL and the predominant cell being the neutrophil. Polarized light microscopy usually reveals rhomboid, square, or rod-like crystals with weak positive birefringence inside tissue fragments and fibrin clots and in neutrophils (Fig. 327-2). CPPD crystals may coexist with MSU and apatite in some cases.

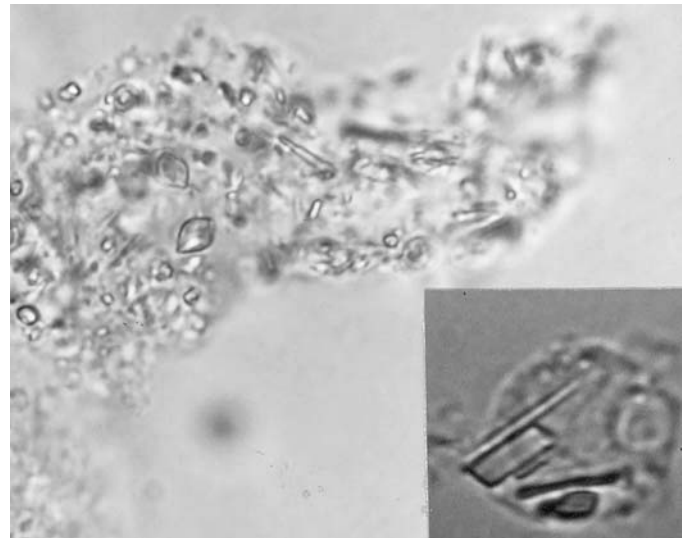


FIGURE 327-2 Intracellular and extracellular calcium pyrophosphate dihydrate crystals, as seen in a fresh preparation of synovial fluid, illustrate rectangular, rod-shaped, and rhomboid weakly positive birefringent crystals (compensated polarized light microscopy; 400×).

Rx CPPD DEPOSITION DISEASE

Untreated acute attacks may last a few days to as long as a month. Treatment by joint aspiration and NSAIDs or by intraarticular glucocorticoid injection may result in return to prior status in ≤10 days. For patients with frequent recurrent attacks of pseudogout, daily prophylactic treatment with low doses of colchicine may be helpful in decreasing the frequency of the attacks. Severe polyarticular attacks usually require short courses of glucocorticoids. Unfortunately, there is no effective way to remove CPPD deposits from cartilage and synovium. Uncontrolled studies suggest that the administration of antimalarial agents or even methotrexate may be helpful in controlling persistent synovitis. Patients with progressive destructive large-joint arthropathy may require joint replacement.

CALCIUM APATITE DEPOSITION DISEASE

PATHOGENESIS

Apatite is the primary mineral of normal bone and teeth. Abnormal accumulation can occur in areas of tissue damage (dystrophic calcification), in hypercalcemic or hyperparathyroid states (metastatic calcification), and in certain conditions of unknown cause (Table 327-3). In chronic renal failure, hyperphosphatemia can contribute to extensive

TABLE 327-3 CONDITIONS ASSOCIATED WITH APATITE DEPOSITION DISEASE

Aging
Osteoarthritis
Hemorrhagic shoulder effusions in the elderly (Milwaukee shoulder)
Destructive arthropathy
Tendinitis, bursitis
Tumoral calcinosis (sporadic cases)
Disease-associated
Hyperparathyroidism
Milk-alkali syndrome
Renal failure/long-term dialysis
Connective tissue diseases (e.g., systemic sclerosis, idiopathic myositis, SLE)
Heterotopic calcification following neurologic catastrophes (e.g., stroke, spinal cord injury)
Heredity
Bursitis, arthritis
Tumoral calcinosis
Fibrodysplasia ossificans progressiva

Note: SLE, systemic lupus erythematosus.

327-4 apatite deposition both in and around joints. Familial aggregation is rarely seen; no association with *ANKH* mutations has been described thus far. Apatite crystals are deposited primarily on matrix vessels. Incompletely understood alterations in matrix proteoglycans, phosphatases, hormones, and cytokines can probably influence crystal formation.

Apatite aggregates are commonly present in synovial fluid in an extremely destructive chronic arthropathy of the elderly that occurs most often in shoulders (Milwaukee shoulder) and in a similar process in hips, knees, and erosive osteoarthritis of fingers. Joint destruction is associated with damage to cartilage and supporting structures, leading to instability and deformity. Progression tends to be indolent, and synovial fluid leukocyte counts are usually $<2000/\mu\text{L}$. Symptoms range from minimal to severe pain and disability that may lead to joint replacement surgery. Whether severely affected patients merely represent an extreme synovial tissue response to the apatite crystals that are so common in osteoarthritis is uncertain. Synovial lining cell cultures exposed to apatite (or CPPD) crystals markedly increase the release of collagenases and neutral proteases, underscoring the destructive potential of abnormally stimulated synovial lining cells.

CLINICAL MANIFESTATIONS

Periarticular or articular deposits may occur and may be associated with acute reversible inflammation and/or chronic damage to the joint capsule, tendons, bursa, or articular surfaces. The most common sites of apatite deposition include bursae and tendons in and/or around the knees, shoulders, hips, and fingers. Clinical manifestations include asymptomatic radiographic abnormalities, acute synovitis, bursitis, tendinitis, and chronic destructive arthropathy. Although the true incidence of apatite arthritis is not known, 30–50% of patients with osteoarthritis have apatite microcrystals in their synovial fluid. Such crystals can frequently be identified in clinically stable osteoarthritic joints, but they are more likely to come to attention in persons experiencing acute or subacute worsening of joint pain and swelling. The synovial fluid leukocyte count in apatite arthritis is usually low ($<2000/\mu\text{L}$), despite dramatic symptoms, with predominance of mononuclear cells.

DIAGNOSIS

Intra- and/or periarticular calcifications with or without erosive, destructive, or hypertrophic changes may be seen on radiographs (Fig. 327-3). These should be distinguished from the linear calcifications typical of CPPD deposition disease.

Definitive diagnosis of apatite arthropathy depends on identification of crystals from synovial fluid or tissue (Fig. 327-3). Individual crystals, which generally contain mostly carbonate substituted apatite, are very small and can be seen only by electron microscopy. Clumps of crystals may appear as 1- to 20- μm shiny intra- or extracellular non-birefringent globules or aggregates that stain purplish with Wright's stain and bright red with alizarin red S. Absolute identification depends on electron microscopy with energy-dispersive elemental analysis, x-ray diffraction, or infrared spectroscopy, but these are usually not required in clinical diagnosis.

Rx CALCIUM APATITE DEPOSITION DISEASE

Treatment of apatite arthritis or periartthritis is nonspecific. Acute attacks of bursitis or synovitis may be self-limiting, resolving in days to several weeks. Aspiration of effusions and the use of either NSAIDs or oral colchicine for 2 weeks or intra- or periarticular injection of a depot glucocorticoid appear to shorten the duration and intensity of symptoms. Periarticular apatite deposits may be resorbed with resolution of attacks. Agents to lower serum phosphate levels may lead to resorption of deposits in renal failure patients receiving hemodialysis. In patients with underlying severe destructive articular changes, response to medical therapy is usually less rewarding.

CaOx DEPOSITION DISEASE

PATHOGENESIS

Primary oxalosis is a rare hereditary metabolic disorder (Chap. 358). Enhanced production of oxalic acid may result from at least two dif-

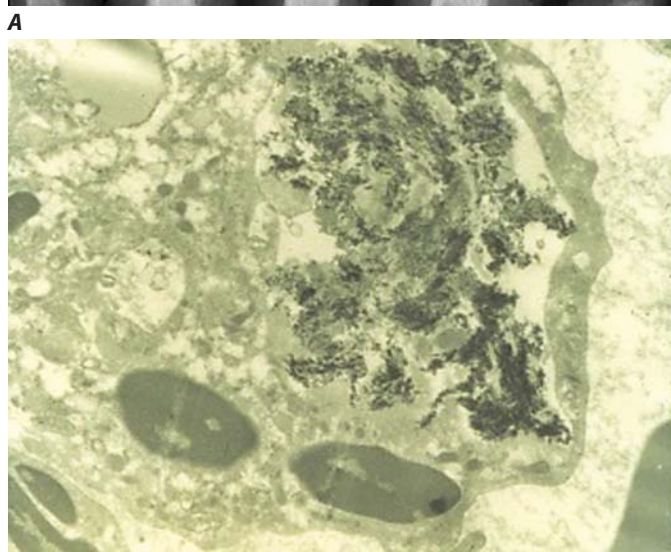
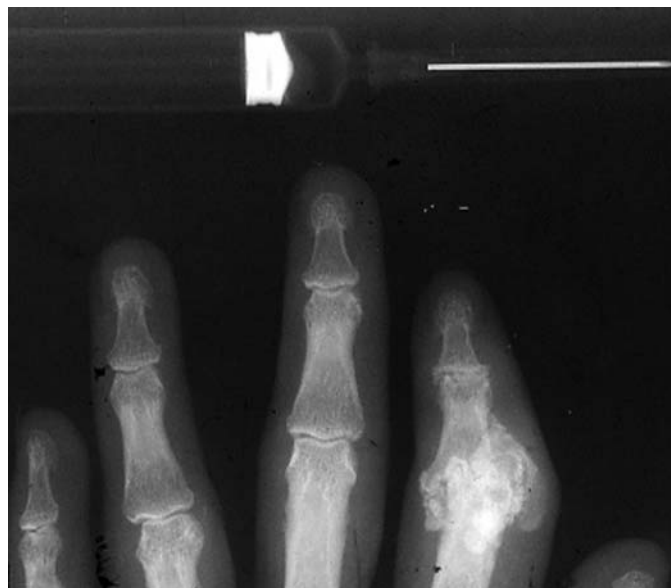


FIGURE 327-3 **A.** Radiograph showing calcification due to apatite crystals surrounding an eroded joint. **B.** An electron micrograph demonstrates dark needle-shaped apatite crystals within a vacuole of a synovial fluid mononuclear cell (30,000 \times).

ferent enzyme defects, leading to hyperoxalemia and deposition of calcium oxalate crystals in tissues. Nephrocalcinosis, renal failure, and death usually occur before age 20. Acute and/or chronic CaOx arthritis and periartthritis may complicate primary oxalosis during later years of illness.

Secondary oxalosis is more common than the primary disorder. It is one of the many metabolic abnormalities that complicate end-stage renal disease. In chronic renal disease, calcium oxalate deposits have long been recognized in visceral organs, blood vessels, bones, and even cartilage. However, it was not until 1982 that such deposits were demonstrated to be one of the causes of arthritis in chronic renal failure. Thus far, reported patients have been dependent on long-term hemodialysis or peritoneal dialysis (Chap. 275), and many had received ascorbic acid supplements. Ascorbic acid is metabolized to oxalate, which is inadequately cleared in uremia and by dialysis. Such supplements are now usually avoided in dialysis programs because of the risk of enhancing hyperoxalosis and its sequelae.

CLINICAL MANIFESTATIONS AND DIAGNOSIS

CaOx aggregates can be found in bone, articular cartilage, synovium, and periarticular tissues. From these sites, crystals may be

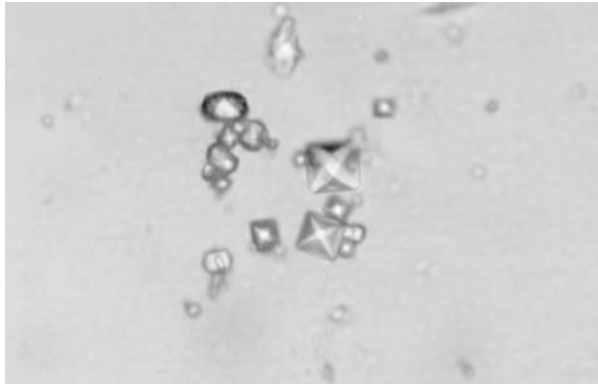


FIGURE 327-4 Bipyramidal and small polymorphic calcium oxalate crystals from synovial fluid are classical finding in CaOx arthropathy (ordinary light microscopy; 400 \times).

shed, causing acute synovitis. Persistent aggregates of CaOx can, like apatite and CPPD, stimulate synovial cell proliferation and enzyme release, resulting in progressive articular destruction. Deposits have been documented in fingers, wrists, elbows, knees, ankles, and feet.

Clinical features of acute CaOx arthritis may not be distinguishable from those due to sodium urate, CPPD, or apatite. Radiographs may reveal chondrocalcinosis or soft tissue calcifications. CaOx-induced synovial effusions are usually noninflammatory, with <2000 leukocytes/ μL , or mildly inflammatory. Neutrophils or mononuclear cells can predominate. CaOx crystals have a variable shape and variable birefringence to polarized light. The most easily recognized forms are bi-

pyramidal, have strong birefringence (Fig. 327-4), and stain with alizarin red S. **327-5**

Rx CALCIUM OXALATE DEPOSITION DISEASE

Treatment of CaOx arthropathy with NSAIDs, colchicine, intraarticular glucocorticoids, and/or an increased frequency of dialysis has produced only slight improvement. In primary oxalosis, liver transplantation has induced a significant reduction in crystal deposits (Chap. 358).

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FURTHER READINGS

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