Numerous drugs are available to abort or prevent acute attacks of arthritis and mobilize tophaceous deposits. Their use is important, because many aspects of the disease are related to the duration and severity of the hyperuricemia. Generally, gout does not materially shorten the life span, but it may impair the quality of life.

Calcium Pyrophosphate Crystal Deposition Disease (Pseudo-Gout)

Calcium pyrophosphate crystal deposition disease (CPPD), also known as *pseudo-gout* and *chondrocalcinosis*, usually occurs in individuals older than 50 years of age and becomes more common with increasing age, rising to a prevalence of 30% to 60% in those 85 years or older. The sexes and races are equally affected. CPPD is divided into sporadic (idiopathic), hereditary, and secondary types. In an autosomal dominant variant the crystals develop relatively early in life and are associated with severe osteoarthritis. The disease is caused by germline mutations in the pyrophosphate transport channel. The secondary form is associated with various disorders, including previous joint damage, hyperparathyroidism, hemochromatosis, hypomagnesemia, hypothyroidism, ochronosis, and diabetes.

Pathophysiology. The basis for crystal formation is not known but studies suggest that articular cartilage proteoglycans, which normally inhibit mineralization, are degraded allowing crystallization around chondrocytes. As in gout, inflammation is caused by activation of the inflammasome in macrophages (Fig. 26-46).

MORPHOLOGY

The crystals first develop in the articular cartilage, menisci, and intervertebral discs, and as the deposits enlarge they may rupture and seed the joint. The crystals form chalky, white friable deposits, which are seen histologically in stained preparations as oval blue-purple aggregates (Fig. 26-48*A*). Individual crystals are rhomboid, 0.5 to 5 μm in greatest dimension (Fig. 26-48*B*) and are positively birefringent. Inflammation, if present, is usually milder than in gout.

CPPD is frequently asymptomatic. However, it may produce acute, subacute, or chronic arthritis that can be confused with osteoarthritis or rheumatoid arthritis. The joint involvement may last from several days to weeks and may be monoarticular or polyarticular; the knees, followed by the wrists, elbows, shoulders, and ankles, are most commonly affected. Ultimately, approximately 50% of affected individuals experience significant joint damage. Therapy is supportive. There is no known treatment that prevents or slows crystal formation.

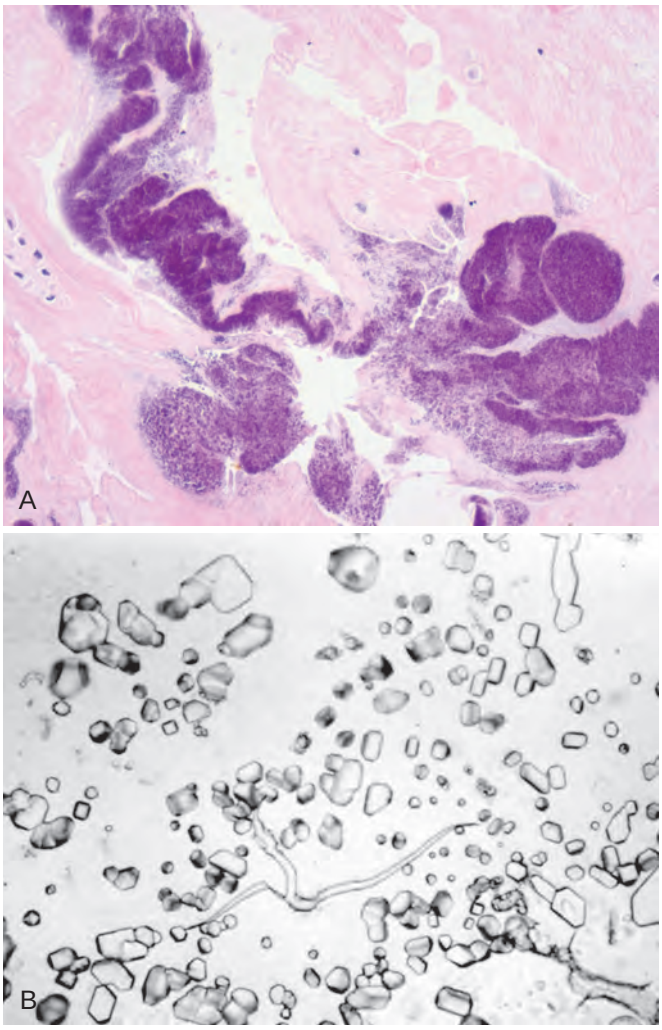

Figure 26-48 Pseudogout. **A,** Deposits are present in cartilage and consist of amorphous basophilic material. **B,** Smear preparation of calcium pyrophosphate crystals.

KEY CONCEPTS

Arthritis

- **Osteoarthritis (degenerative joint disease)**, the most common disease of joints, is a degenerative process of articular cartilage in which matrix breakdown exceeds synthesis. Inflammation is minimal and typically secondary. Local production of inflammatory cytokines may contribute to the progression of joint degeneration.
- **Rheumatoid arthritis (RA)** is a chronic autoimmune inflammatory disease that affects mainly small joints, but can be systemic. RA is caused by a cellular and humoral immune response against self-antigens, particularly citrullinated proteins. TNF plays a central role and antagonists against TNF are of clinical benefit.
- **Seronegative spondyloarthropathies** are a heterogeneous group of likely autoimmune arthritides that preferentially involve the sacroiliac and vertebral joints and are associated with HLA-B27.
- **Suppurative arthritis** describes direct infection of a joint space by bacterial organisms.
- **Lyme disease** is a systemic infection by *Borrelia burgdorferi* which manifests, in part, as an infectious arthritis, possibly with an autoimmune component in chronic stages.
- **Gout and pseudogout** result from inflammatory responses triggered by precipitation of urate or calcium pyrophosphate, respectively.