frequency by the hip, shoulder, elbow, wrist, and sternoclavicular joints. The axial joints are more often involved in drug users. Joint aspiration is diagnostic if it yields purulent fluid in which the causal agent can be identified. Prompt recognition and effective antimicrobial therapy can prevent joint destruction.

Mycobacterial Arthritis

Mycobacterial arthritis is a chronic progressive monoarticular infection caused by *M. tuberculosis,* which occurs in all age groups, especially adults. It usually develops as a complication of adjoining osteomyelitis or after hematogenous dissemination from a visceral (usually pulmonary) site of infection. Onset is insidious and causes gradual progressive pain. Systemic symptoms may or may not be present. Mycobacterial seeding of the joint induces the formation of confluent granulomas with central caseous necrosis. The affected synovium may grow as a pannus over the articular cartilage and erode the bone along the joint margins. Chronic disease results in fibrous ankylosis and obliteration of the joint space. The weight-bearing joints are usually affected, especially the hips, knees, and ankles in descending order of frequency.

Lyme Arthritis

Lyme arthritis is caused by infection with the spirochete *Borrelia burgdorferi*, which is transmitted by deer ticks of the *Ixodes ricinus* complex. It is the leading arthropod borne disease in the United States. In its classic form, Lyme disease progressively involves multiple organ systems, as outlined in Chapter 8. The initial infection of the skin is followed within several days or weeks by dissemination of the organism to other sites, especially the joints.

Approximately 60% to 80% of untreated individuals with the disease develop arthritis during the late stage. The arthritis primarily involves large joints, especially the knees, shoulders, elbows, and ankles in descending order of frequency. Usually one or two joints are affected at a time, and the attacks last for a few weeks to months, migrating to new sites. Spirochetes can only be identified in about 25% of joints with arthritis but the diagnosis can be confirmed by serologic testing for anti-*Borrelia* antibodies. The majority of individuals respond to antibiotic therapy.

A chronic arthritis that is antibiotic refractory develops in approximately 10% of affected individuals. In many of these patients, *Borrelia* cannot be detected in the joint fluid even by PCR. It has been proposed that cellular (especially T_H1) and humoral responses to *Borrelia* outer surface protein A may initiate an autoimmune arthritis, but this is not proven.

Infected synovium exhibits a chronic synovitis marked by synoviocyte hyperplasia, fibrin deposition, mononuclear cell infiltrates (especially CD4+ T cells), and onion-skin thickening of arterial walls. The morphology in severe cases can closely resemble that of rheumatoid arthritis.

Viral Arthritis

Arthritis can occur in the setting of a variety of viral infections, including alphavirus, parvovirus B19, rubella, Epstein-Barr virus, and hepatitis B and C viruses. The manifestations of the arthritis range from acute to subacute symptoms. The joint symptoms may be caused by direct infection of the joint by the virus, as seen in rubella and some alphavirus infections, or by an autoimmune reaction generated by the infection, as is seen in other forms of reactive or post-infectious arthritides. A variety of rheumatic conditions, including reactive arthritis, psoriatic arthritis, and septic arthritis, may develop in individuals infected with HIV. The pathogenesis of some of these forms of HIV-associated chronic arthritis is probably autoimmune. Antiretroviral therapies for HIV have reduced the severity of HIV-associated arthritis.

Crystal-Induced Arthritis

Articular crystal deposits are associated with a variety of acute and chronic joint disorders. Endogenous crystals shown to be pathogenic include monosodium urate *(gout),* calcium pyrophosphate dehydrate *(pseudogout),* and basic calcium phosphate. Exogenous crystals, such as corticosteroid ester crystals and talcum, and the biomaterials polyethylene and methyl methacrylate, may also induce joint disease. Silicone, polyethylene, and methyl methacrylate are used in prosthetic joints, and their debris that accumulates with long use and wear may result in local arthritis and failure of the prosthesis. Endogenous and exogenous crystals produce disease by triggering a cytokine-mediated cascade that destroys cartilage.

Gout

Gout is marked by transient attacks of acute arthritis initiated by crystallization of monosodium urate within and around joints. Gout can be divided into primary and secondary forms (Table 26-7), both sharing the common feature of hyperuricemia. In the primary form (90% of cases), gout is the major manifestation of the disease and the cause is usually unknown. In secondary gout (10% of cases), uric acid is increased because of a known underlying disease that usually dominates the clinical picture.

Table 26-7 Classification of Gout

Clinical Category	Uric Acid Production	Uric Acid Excretion
Primary Gout (90%)		
Unknown enzyme defects (85%-90%)	↑ (majority) ↑↑ (minority) Normal	Normal ↑ ↓
Known enzyme defects (e.g., partial HGPRT deficiency)	↑	Normal
Secondary Gout (10%)		
Increased nucleic acid turnover (e.g., leukemia)	↑↑	↑
Chronic renal disease	Normal	↓
Congenital (e.g., Lesch-Nyhan syndrome HGPRT deficiency)	↑↑	↑

HGPRT, Hypoxanthine guanine phosphoribosyl transferase.