and knees. Uncommonly the upper spine is involved, but the lumbosacral region and hips are usually spared.

Involved joints are swollen, warm, painful, and particularly stiff when rising in the morning or following inactivity. The typical patient has progressive joint enlargement, decreased range of motion evolving to complete ankylosis, with the greatest damage occurring in the first 4 or 5 years. Approximately 20% of affected individuals enjoy periods of partial or complete remission, but the symptoms inevitably return and involve previously unaffected joints. A minority of individuals (10%) have an acute onset over several days with severe symptoms and polyarticular involvement.

Inflammation in the tendons, ligaments, and occasionally the adjacent skeletal muscle frequently accompanies the arthritis and produces the characteristic radial deviation of the wrist, ulnar deviation of the fingers and flexion-hyperextension of the fingers (swan-neck deformity, boutonnière deformity). The end result is a joint that has no stability and minimal or no range of motion. Large synovial cysts, like the *Baker cyst* in the posterior knee, may develop as the increased intra-articular pressure causes herniation of the synovium. Radiographic hallmarks are joint effusions and juxta-articular osteopenia with erosions and narrowing of the joint space and loss of articular cartilage (Fig. 26-45).

The presence of multisystem involvement must be distinguished from other forms of chronic arthritis (lupus, scleroderma, Lyme disease). The diagnosis of RA is supported by (1) characteristic radiographic findings, (2) sterile, turbid synovial fluid with decreased viscosity, poor mucin clot formation, and inclusion-bearing neutrophils, and (3) the combination of rheumatoid factor and anti-CCP antibody (80% of patients).

The treatment of rheumatoid arthritis is aimed at relieving the pain and inflammation, and slowing or arresting the relentless joint destruction. Therapies include corticosteroids, synthetic and biologic disease-modifying drugs such as methotrexate, and, most notably, antagonists of TNF. Such drugs prevent or slow joint destruction, which is the greatest source of disability, and have altered the natural history of the disease for the better. However, anti-TNF agents are not curative, and patients must be maintained on TNF antagonists to avoid disease flares. Other biologic agents that interfere with T and B lymphocyte responses are also approved therapies.

Long-term complications include *systemic amyloidosis* (Chapter 6) in 5% to 10% of patients and infection with opportunistic organisms in patients who receive long-term anti-TNF or other immunosuppressive agents.

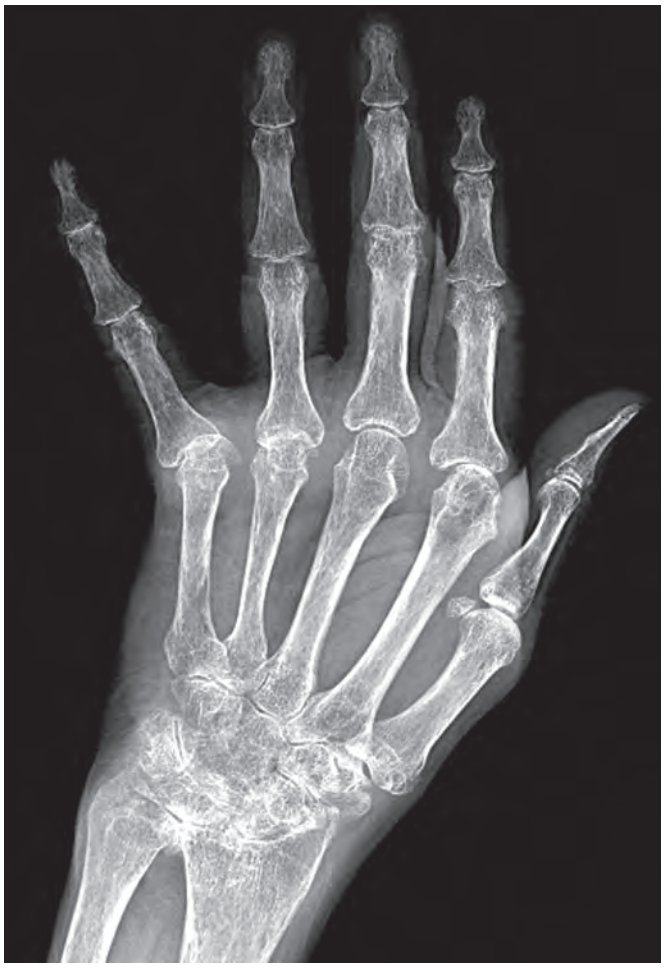

Figure 26-45 Rheumatoid arthritis of the hand. Characteristic features include diffuse osteopenia, marked loss of the joint spaces of the carpal, metacarpal, phalangeal, and interphalangeal joints, periarticular bony erosions, and ulnar drift of the fingers.

Juvenile Idiopathic Arthritis

Juvenile idiopathic arthritis (JIA) is a heterogeneous group of disorders of unknown cause that present with arthritis before age 16 and persist for at least 6 weeks. The prevalence is 30,000 to 50,000 in the United States. Compared to RA, in JIA (1) oligoarthritis is more common, (2) systemic disease is more frequent, (3) large joints are affected more often than small joints, (4) rheumatoid nodules and rheumatoid factor are usually absent, and (5) antinuclear antibody (ANA) seropositivity is common. The pathogenesis is unknown but similar to adult RA; risk factors include *HLA* and *PTPN22* variants. Also like adult RA, damage in JIA appears to be caused by T_H1 and T_H17 cells and the mediators IL-1, IL-17, TNF, and IFN-γ.

Attempts at subclassification of JIA are based on clinical (e.g., oligoarticular, systemic) and laboratory (ANA, rheumatoid factor titers) variables. Some of these subgroups (e.g., systemic, polyarticular rheumatoid factor positive; enthesitis-related, which refers to involvement of sites of ligament and cartilage insertion into bone; oligoarticular) seem to represent defined entities while others (e.g., polyarticular rheumatoid factor negative; psoriatic) remain heterogeneous. Treatment consists of similar regimens as adult RA with some success using an IL-6 receptor antibody in the systemic form. Long-term prognosis of JIA is very variable. Although many affected individuals may have chronic disease, only about 10% develop serious functional disability.

Seronegative Spondyloarthropathies

The spondyloarthropathies are also a heterogeneous group of disorders that are unified by the following features:

- Pathologic changes in the ligamentous attachments rather than synovium