The Rheumatic Diseases: A Primer

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Objectives

- To understand the importance and impact of these conditions on society and the health-care system
- To appreciate that such patients make up a significant proportion of an orthopedic practice
- To appreciate the protean nature of these disorders and their varied pathophysiology
- To understand the systematic approach to the differential diagnosis of these conditions presented
- To overview the diagnostic evaluation of systemic rheumatic diseases

Key Points

- Chronic rheumatic diseases represent a broad category of conditions that share a common feature: the destruction of cartilage and its consequences.
- While these conditions differ in their pathophysiology, the final common target is often the joint; hence, such patients frequently require orthopedic surgery.
- Classification of rheumatic diseases follows this organization: osteoarthritis; disorders of the synovium (rheumatoid arthritis), connective tissue diseases (systemic lupus erythematosus, antiphospholipid syndrome, systemic sclerosis, inflammatory disease of the muscle), spondyloarthritis (ankylosing spondylitis, psoriatic arthritis, enteropathic arthropathies, reactive arthritis, etc.), vasculitides (polymyalgia rheumatica/temporal arteritis, polyarteritis nodosa, microscopic polyangiitis, granulomatosis with polyangiitis, eosinophilic granulomatosis with polyangiitis, cryoglobulinemic vasculitis), metabolic bone disease (osteoporosis), crystal-induced arthropathies (gout, calcium pyrophosphate-associated arthropathy), infectious arthritis, sarcoidosis

Introduction

Estimates of the prevalence of arthritis and the rheumatic diseases in general make evident the enormous impact that these conditions have on the US populace and the health-care system in general. More than 21% of US adults (46 million people) currently report physician-diagnosed arthritis. The National Arthritis Data Workgroup, an impressive collaborative effort from the Centers for Disease Control and Prevention, the National Institutes of Health, the American College of Rheumatology, and the Arthritis Foundation, has published analyses that project an increase of physician-diagnosed arthritis to nearly 67 million people (an increase of 40%) by the year 2030 [1]. While the majority of this health burden arises as a consequence of osteoarthritis, the entire span of the rheumatic diseases, such as rheumatoid arthritis, psoriatic arthritis, juvenile arthritis, spondyloarthropathies, enteropathic arthritis, systemic lupus erythematosus, systemic sclerosis, and primary Sjogren's syndrome, contributes to the impact of this class of conditions. Already the leading cause of disability in the nation, the number of people with arthritis and arthritis-attributable limitation in activity is a serious public health issue. Such observa-

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tions highlight the importance of effective interventions and programs to reduce the impact (loss of productivity, costs of therapy) of these chronic diseases. Ultimately, orthopedic intervention is required in many of these individuals to address the main issues of palliation of pain, inflammation, and further structural damage and disability compromising one's quality of life. Factors such as an increased patient awareness of the benefits of surgery, improvements in surgical techniques, and the desire for an active lifestyle have, in concert with the increasing prevalence of chronic arthritis, fueled the growth in utilization of orthopedic surgery. The orthopedic perspective and contemporary estimates concerning the rates of total joint replacement and spine surgery have been extensively reviewed in Chap. 5. This chapter introduces the broader spectrum of the rheumatic diseases as viewed by the rheumatologist as such patients frequently require orthopedic intervention. Beginning with a review of the relevant pathobiology, a concise primer of the essential diseases is then presented.

Pathological Considerations

The elemental pathological process leading to orthopedic surgery is damage and gradual loss of the articular cartilage. However, all structures within the joint including the bones and connective tissue are affected. Osteoarthritis involves the joint in an asymmetric, localized pattern of involvement, with focal stress across the joint. This leads to misalignment and progressive alterations in load bearing relationships of the joint, resulting in the radiographic joint space narrowing and chronic joint damage. The structural changes occur in concert with biochemical abnormalities that ensue within the cartilage component, the underlying subchondral bone, joint capsule, and synovial membrane. Microscopically, biomechanical properties of the normal cartilage contain two main components: extracellular matrix (rich in type II, IX, and XI collagens and proteoglycans) and the chondrocytes lying within the matrix, responsible for maintaining homeostatic synthesis of the extracellular matrix components. The abnormal mechanical stress that occurs in OA causes alterations in chondrocyte metabolism and incites local inflammation by inducing synthesis of proteases, such as matrix metalloproteinase (MMP)-1, MMP-8, and MMP-13, and inflammatory mediators, such as interleukin (IL)-8, IL-6, prostaglandin E2, and nitric oxide [2]. The joint damage results from the metabolic imbalance due to accelerated cartilage degradation coupled with an insufficient reparative response. These processes incite localized tissue response consisting of inflammation of the joint lining and further loss of mechanical properties of the affected joint. Owing to the synthesis of metalloproteinases, there is gradual loss of the matrix components. Alterations of the proteoglycan content and structure then follow, and with continued deterioration in the cartilage and its load bearing capacity, stiffness and pain ensue, as nociceptive and proprioceptive receptors in the periosteum are activated due to the loss of the protective layer of the articular cartilage. Bone remodeling occurs in the underlying subchondral bone, causing sclerosis of the bone, formation of bone cysts, increased subchondral plate thickness, and reactive osteophyte formation at joint margins as a result of abnormal reparative process [3, 4].

Osteoarthritis is the most common cause of end-stage arthritis. Osteoarthritis may be primary, due to biochemical changes in the cartilage, or secondary to systemic disease affecting the cartilage, joint damage from pre-existing inflammatory joint disease, or trauma. It is a heterogeneous disease with various etiologies. Mechanical overload and imbalances lead to further cartilage degradation, processes that culminate in a failure of the mechanical functioning of the surrounding normal structures. Important adaptive responses such as subchondral sclerosis and osteophyte formation occur in response to joint overload, and, if chronically present, cyst formation in the sub-articular bone may also result. Over time the osteophytes or bone spurs will lead to restricted range of motion.

Inflammatory arthritis, by contrast, is a constellation of diseases that target the synovium. Included in this class of disorders are such conditions as rheumatoid arthritis (RA), psoriatic arthritis (PsA), and the spondyloarthritis (SpA). Common to all is the release of inflammatory mediators by the synovium leading to cartilage destruction. In contrast to osteoarthritis, mechanical overload is not a primary mechanism; as such, bone sclerosis or osteophyte formation is not seen. Rather, the inflammatory synovitis leads to a loss of cartilage matrix, marginal bony erosions, destruction of the joint capsule, and osteopenia.

Trauma is also an important cause of joint destruction. Post-traumatic arthritis is initiated by cartilage damage at the time of injury or by secondary mechanical imbalances that result from fractures of juxta-articular bone. Abnormal loading conditions will subsequently lead to a wear-and-tear form of cartilage damage.

Osteonecrosis, also termed avascular necrosis, is another entity that may lead to joint arthritis. In this process the blood supply to the bone is compromised leading to necrosis of the bone supporting the articular surface. The most commonly affected joints are the hip, shoulder, and knee. As the disease progresses, the necrotic bone may collapse leading to the loss of articular integrity and progressive cartilage deterioration. Avascular necrosis of the bone is frequently seen in patients with rheumatic disease who have been exposed to glucocorticoids.

Other conditions that may lead to joint damage include storage and deposition disorders (hemochromatosis, alkaptonuria, Wilson's disease, Gaucher's disease), crystal deposition diseases (chondrocalcinosis, gout), tumor (synovial chondromatosis), and infectious (post-septic) and bleeding disorders (hemophilia).

Owing to the prominent involvement of joints and the musculoskeletal system, patients who acquire these often multi-systemic conditions frequently require orthopedic intervention. The protean clinical manifestations of these diseases, coupled with important medication-related management considerations, present challenges encompassing the span of perioperative medical practice. Indeed such patients are amongst the most challenging encountered in the perioperative setting [5, 6].

Laboratory Considerations

The clinical laboratory can be of great help in the diagnosis of rheumatic conditions. Although laboratory tests are often informative, they are rarely definitive or diagnostic. Laboratory examinations must be used in conjunction with a complete history and physical and radiographic examinations. When diagnosing a disorder, one of the most important considerations is to determine whether the cause is inflammatory (and frequently systemic) or noninflammatory. Inflammatory rheumatic conditions often have an acute phase response. The acute phase response occurs after many other events, including infections, trauma, immune diseases, crystalline deposition, and malignancy. Acute phase reactants such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are often elevated in systemic rheumatic diseases. Moderate elevations of CRP occur in most connective tissue diseases (1–10 mg/dL). Very high levels are seen in bacterial infections and systemic vasculitis (15–20 mg/dL). Diabetes, obesity, and cigarette smoking can increase CRP levels in variable amounts. CRP levels fall when inflammation subsides. Since a substantial stimulus is required for CRP elevation, a normal value does not exclude an inflammatory process; thus, some clinicians prefer sending ESR concomitantly with CRP. Normal ESR is considered 0–15 for males and 0–20 for females. ESR increases with age; thus, "normal" levels are variable with levels up to 40 mm/hour common in healthy elderly people. Thus, ESR and CRP are neither diagnostic nor specific though are often helpful in evaluating patients with systemic inflammatory/rheumatic conditions. Table 4.1 summarizes useful laboratory tests for the diagnoses of rheumatic diseases. These may be used in conjunction with the signs and symptoms to diagnose rheumatic conditions. Each of these is explained in detail along with the description of the individual diseases.

Table 4.1 Useful laboratory tests for rheumatic diseases

Tests/autoantibodies	Comments
Erythrocyte sedimentation rate (ESR)	Acute phase reactant often elevated in systemic inflammatory diseases
C-reactive protein (CRP)	Acute phase reactant often elevated in systemic inflammatory diseases
Rheumatoid factor (RF)	Rheumatoid arthritis and sometimes detected in Sjogren's syndrome
Anti-cyclic citrullinated peptide (anti-CCP)	Rheumatoid arthritis
Anti-double-stranded DNA (ds-DNA)	Systemic lupus erythematosus (SLE)
Antinuclear antibodies (ANA)	Nearly 100% of SLE patients are positive Also seen in other connective tissue diseases
Complements – C3 and C4	Decreases in C3 and C4 levels precede SLE flares
Anti-Ro (SS-A)	Sjogren's syndrome
Anti-La (SS-B)	Sjogren's syndrome
Anti-Smith	SLE
Anti-RNP	SLE, mixed connective tissue disease (MCTD)
Lupus anticoagulant	Antiphospholipid syndrome
Anti-cardiolipin antibodies IgG, A, and M	Antiphospholipid syndrome
Beta-2 glycoprotein IgG, A, and M	Antiphospholipid syndrome
Anti-DNA topoisomerase I (Scl-70)	Scleroderma
Anti-centromere antibodies	Scleroderma
Anti-RNA polymerase III	Scleroderma
Anti-Jo 1, Anti-Mi2, Anti-SRP, etc.	Dermatomyositis/polymyositis
HLA–B 27	Spondyloarthritis
Anti- neutrophil cytoplasmic antibodies (ANCA)	Vasculitides
Angiotensin-converting enzyme (ACE)	Elevated levels detected in sarcoidosis

The Rheumatic Diseases

Box 4.1 presents a general classification of the rheumatic diseases.

Osteoarthritis (OA)

The most common form of arthritis, osteoarthritis, is a heterogeneous group of common conditions that share similar pathological and radiographic features, specifically loss of articular cartilage. It should be considered, furthermore, as an organ failure of the synovial joint, driven by a primary defect in any of its supporting tissues (ligaments, meniscus, subchondral bone, periarticular muscles, synovium, nerves, or articular cartilage) [7]. There are many pathophysiological mechanisms that alter

Box 4.1 Classification of the Rheumatic Diseases

- Osteoarthritis
- Disorders of the synovium
  - Rheumatoid arthritis
- Connective tissue diseases
  - Systemic lupus erythematosus
  - Antiphospholipid syndrome
  - Systemic sclerosis
  - Inflammatory disease of the muscle
- Spondyloarthritis
  - Axial spondyloarthritis
    - Ankylosing spondylitis
    - Nonradiographic axial spondyloarthritis
  - Peripheral spondyloarthritis
  - Psoriatic arthritis
  - Enteropathic arthropathies
  - Reactive arthritis
- Vasculitides
  - Polymyalgia rheumatica/temporal arteritis
  - Polyarteritis nodosa
  - Microscopic polyangiitis
  - Eosinophilic granulomatosis with polyangiitis (Churg-Strauss)
  - Granulomatosis with polyangiitis (Wegener's granulomatosis)
  - Cryoglobulinemic vasculitis
- Metabolic bone disease
  - Osteoporosis
- Crystal-induced arthropathies
  - Gout
  - Calcium pyrophosphate-associated arthropathy
- Infectious arthritis
- Other
  - Sarcoidosis

the relationship between mechanical factors and tissue response of the synovial joint; however, in the end stage of the disease, all components of the joint fail. An age-related disorder, OA, is uncommon before age 40 but increases in prevalence thereafter; by age 70 most people have pathological changes of OA though they may not be symptomatic. Other risk factors include female gender, ethnicity (>blacks), genetic predisposition, obesity (especially for knee OA), and trauma. The causes for primary or idiopathic osteoarthritis remain unclear. Research has focused on the intra-articular alterations involving the articular cartilage and subchondral bone, and considerable interest has arisen in the role of the neuromuscular unit involved in joint motion, stability, and proprioception as contributing to the progression and/or predisposition to the development of OA [8, 9].

Osteoarthritis is a focal disease not affecting all joints equally; even within a given joint, the involvement may be patchy and asymmetric. Its pathogenesis involves an incongruence between normal cartilaginous degradative and repair mechanisms, which results in a net loss of cartilage, bony hypertrophy, and osseous outgrowths (osteophytes). Its primary symptoms are use-related joint pain and stiffness (gelling). On physical examination, some combination of joint tenderness, crepitus, bony enlargement, malalignment, decreased range of motion, and joint effusion are usually noted. Treatment is mainly symptomatic (NSAIDs, analgesics, intra-articular injections). In those with severe disease, total joint arthroplasty is the only definitive therapy. Radiographic findings include asymmetric joint space narrowing, subchondral sclerosis and cystic change, and marginal osteophytes (bony spurs) (Figs. 4.1 and 4.2). When the

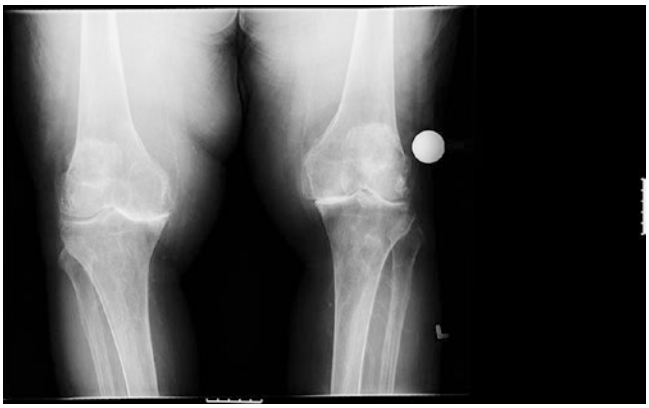

Fig. 4.1 Radiograph of osteoarthritis in knees: varus deformity. X-ray of bilateral knees showing advanced, severe bilateral degenerative arthrosis most marked in the medial compartments bilaterally where there is bone on bone apposition. Tricompartmental osteophytosis is present. Bilateral varus deformity is noted

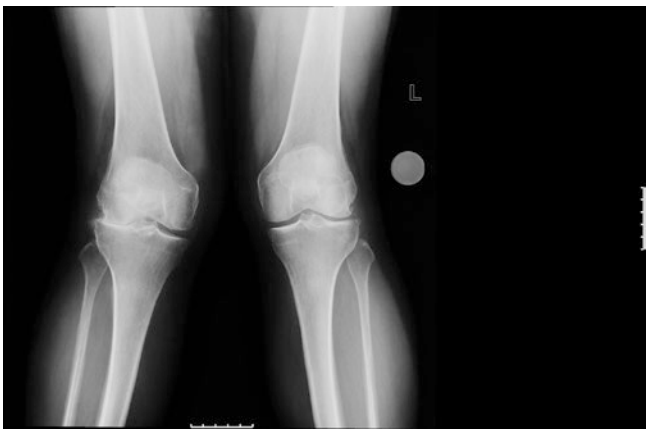

Fig. 4.2 Radiograph of osteoarthritis in knees: valgus deformity. *Right knee* shows severe degenerative arthrosis with tricompartmental osteophytes and lateral bone-on-bone apposition with marked valgus deformity. *Left knee* shows moderate degenerative arthrosis with small joint line osteophytes and moderate lateral compartment narrowing with valgus deformity

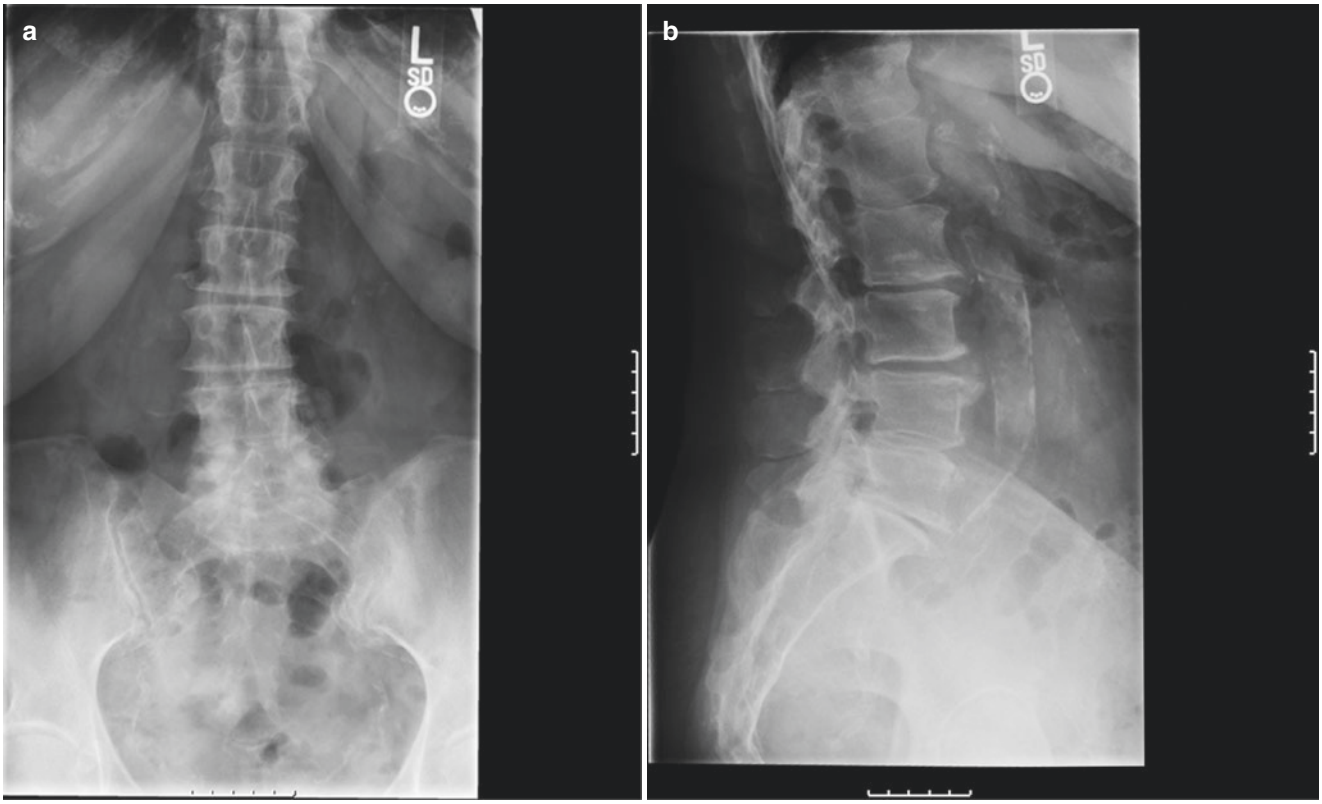

Fig. 4.3 (**a**, **b**) Radiograph of osteoarthritis of lumbar spine. There is a mild curvature of the lumbar spine convex right with multilevel degenerative disk disease with disk space narrowing, endplate sclerosis, and osteophytes at L4–L5 and L5–S1

spine is predominantly involved, disk degeneration and facet joint arthritis result in symptomatic stenosis, necessitating decompression (and fusion) surgery in order to alleviate symptoms and restore a functional activity (Fig. 4.3a, b).

Disorders of the Synovium

Rheumatoid arthritis (RA) is the prototypical disorder primarily affecting the synovium. Whereas the normal synovium consists of a thin intimal lining layer, one to three cell layers thick, comprised of roughly equal proportions of different cell types (macrophage-like synoviocytes or type A synoviocytes and fibroblast-like synoviocytes or type B synoviocytes), in contrast the synovial tissue in RA is greatly hypertrophied (up to 8–10 cell layers thick) displaying increased numbers of both type A and B synoviocytes accompanied by mononuclear cell infiltration of the sublining below the intima transforming the milieu as the pot of inflammatory cytokines and proteases (Fig. 4.4a, b) [10, 11]. The subintimal region where the blood vessels are located becomes heavily infiltrated with inflammatory cells, including T and B lymphocytes, plasma cells, natural killer cells, macrophages, and mast cells. The hypertrophied synovium transforms into villous-like projections, also called pannus, which protrude into the joint cavity and invade the juxtaposed articular cartilage and underlying bone, resulting in cartilage destruction bone erosions and ultimately compromising the integrity of each component of the joint (Fig. 4.5a, b). The destructive properties of the pannus are a result of (1) increased synthesis of metalloproteinases and other proteinases by synovial fibroblasts and monocytes; (2) chondrocyte activation by key cytokines (IL-1, TNF-α, and TGF-ß), resulting in decrease in collagen and proteoglycan synthesis; and (3) recruitment and differentiation of cells that express an osteoclast phenotype leading to focal bone erosions. It is hypothesized that the osteoclast differentiation from the macrophage lineage results in response to inflammatory mediators and cytokines (L-1, TNF-α, IL-17) produced by fibroblast-like synoviocytes in the rheumatoid synovium [12].

Rheumatoid arthritis is a chronic systemic inflammatory disease, driven by autoantibodies and immunologically overactive cells that primarily target the synovium as well as extra-articular tissues and organs. The etiopathogenesis of RA involves a complex interplay of genetic predisposition and probable environmental factors that trigger a cascade of intra-synovial immune response that perpetuates a pro-inflammatory milieu of cellular and molecular phenomena that lead to erosions of the cartilage and bone. Rheumatoid

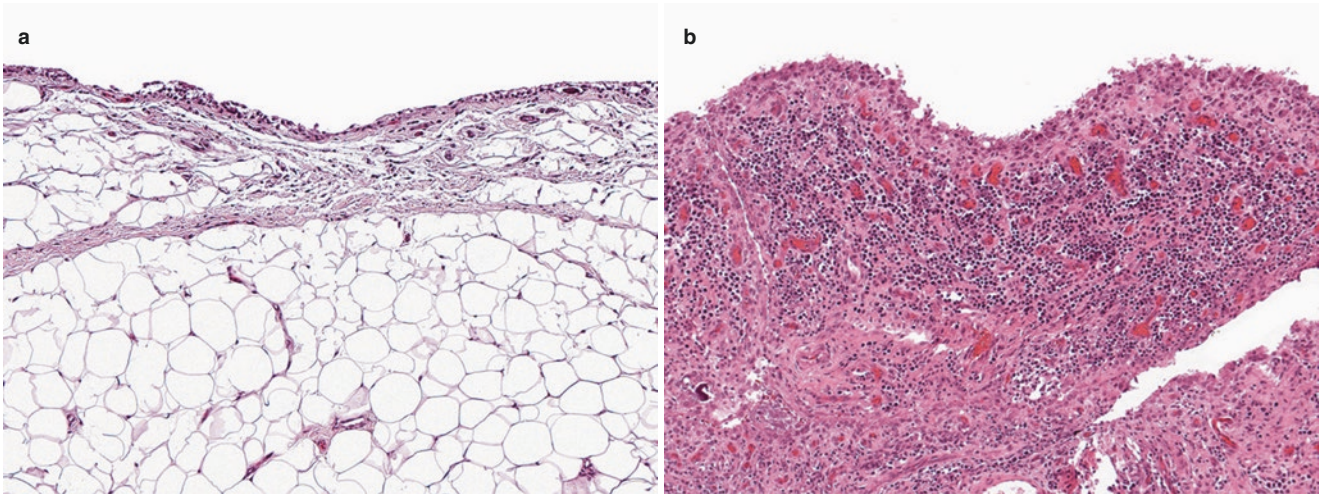

Fig. 4.4 (**a**) Normal synovium: This layer is usually only 1–3 cells thick, comprised of type A macrophage-like synoviocytes and type B fibroblast-like synoviocytes. (**b**) Synovial lining in rheumatoid arthritis: This lining is greatly hypertrophied (8–10 cells thick)

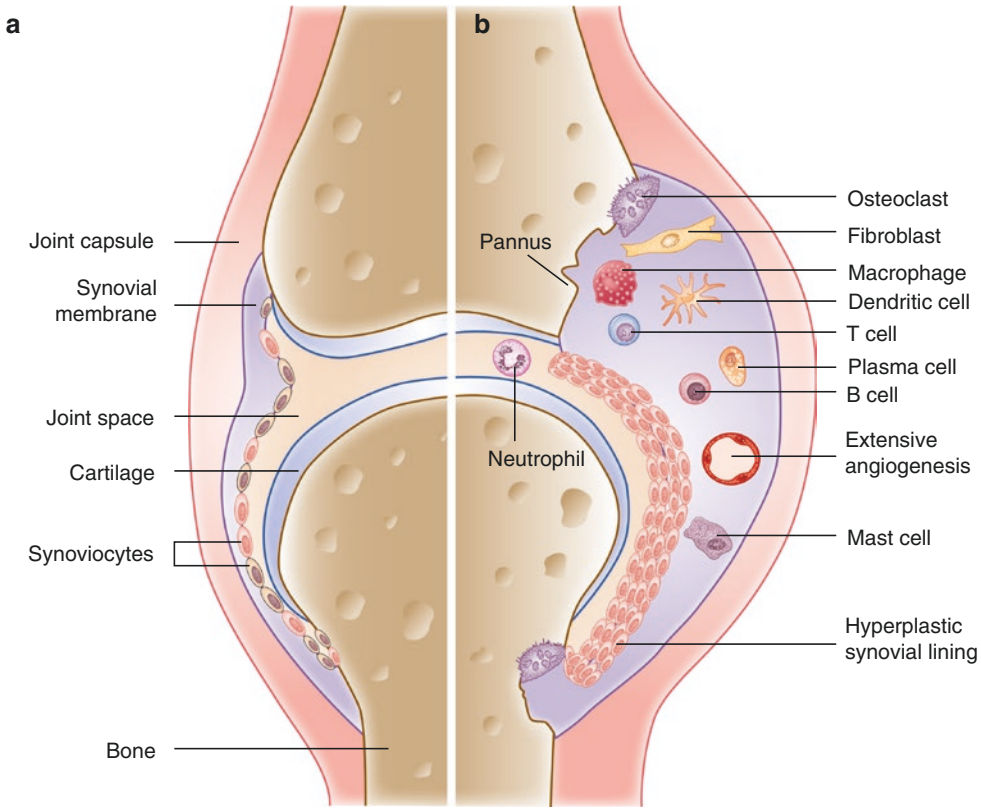

Fig. 4.5 Pannus formation in rheumatoid arthritis. (**a**) Normal synovium with thin intimal layer. (**b**) Synovium in RA showing hypertrophied synovial layer, increased infiltration by inflammatory cells, and angiogenesis. The pannus that develops invades into the joint cavity, articular cartilage, and subchondral bone. (Used with permission of Springer Nature from Strand et al. [37])

arthritis affects females more often than males (RR 3:1). Its peak onset is in the fourth to fifth decade. Usually RA presents insidiously over several weeks to months, with the initial pattern localized to inflammation of the smaller peripheral joints, typically symmetric in distribution, and often with concurrent systemic features of fatigue and generalized malaise. Uncontrolled joint inflammation, characterized by tenderness, swelling, and dysfunction, may lead to larger joint involvement and destruction of synovial joints, followed by deformities and loss of joint function (Fig. 4.6a, b). Extra-articular manifestations may arise but have become less common in the modern therapeutic era.

Products of the human leukocyte antigen (HLA) region of Class II genes of the major histocompatibility complex (MHC) play an important role in the susceptibility and pathogenesis of RA. Individuals who are HLA-DRB4 posi-

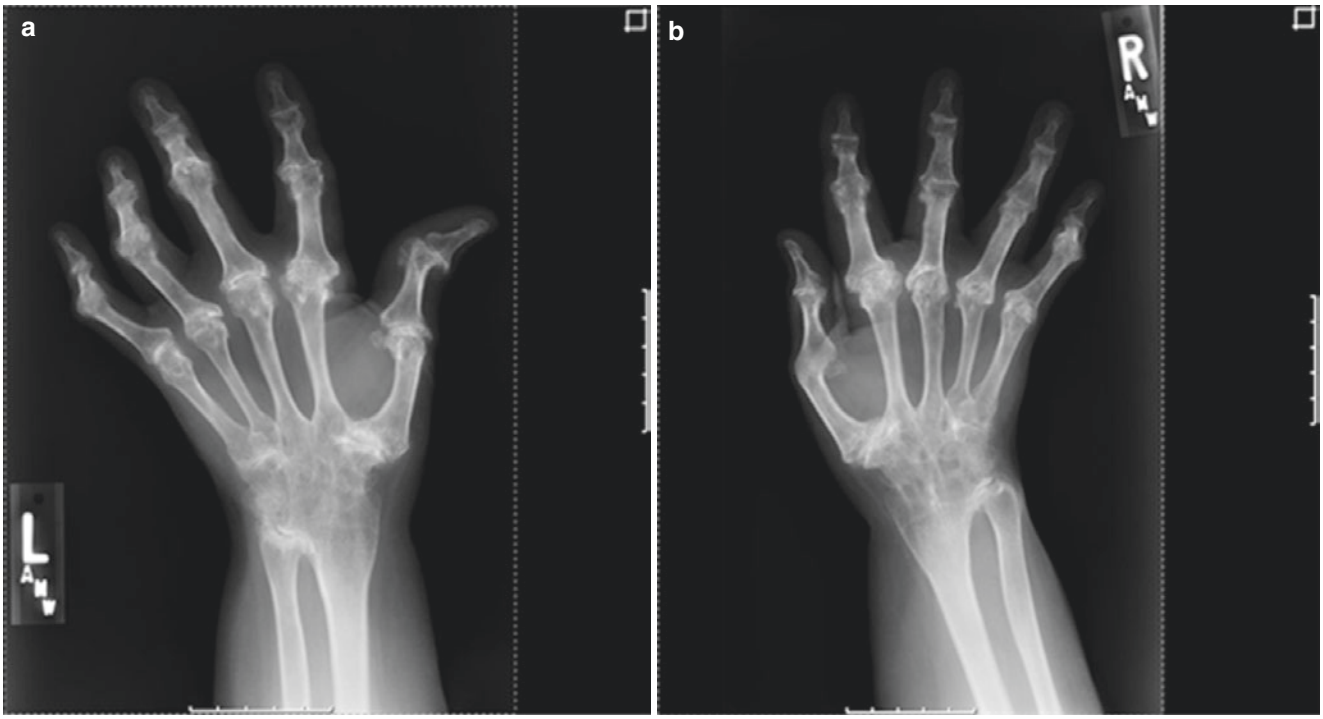

Fig. 4.6 (**a**) Radiographic changes of advanced rheumatoid arthritis. (**b**) Rheumatoid involvement of the metacarpal and proximal interphalangeal joints bilaterally. There is fusion of the carpal joints bilaterally. The radiocarpal joints are fused. The carpal metacarpal joints are fused. Joint space narrowing, mild proliferative changes, and erosions are noted in the MP and PIP joints. There is relative sparing of the DIP joints

tive are more likely to develop severe disease, marked by erosions of the joints, deformity, and disability. The concept of "shared epitope" refers to a common structural domain that consists of 5-amino acid sequence (QKRAA) found on several HLA-DR4 alleles, which has been shown to confer susceptibility to RA [13]. Early in the development of disease, T-lymphocyte infiltration occurs in the synovial tissue, followed by proliferation of the synovial lining; over time synovial infiltration by B cells, macrophages, and fibroblasts follows, and, in response to the production of various chemotactic factors, granulocytes migrate into the joint space discharging pro-inflammatory substances increasing vascular permeability and perpetuating the inflammatory response.

Relevant laboratory studies include markers of the inflammatory response of acute phase reactants (ESR, CRP), rheumatoid factor (RF), and anti-cyclic citrullinated peptide (anti-CCP) antibodies. Rheumatoid factors are autoantibodies directed against the Fc portion of immunoglobulin G (IgG) and are found in 75–80% of RA patients during the course of their illness. The immune complexes deposit into joints and tissues, exacting inflammation and damage. RF lacks specificity as levels may be elevated in certain infectious states (hepatitis, human immunodeficiency virus (HIV), endocarditis), malignancy (multiple myeloma), and also other connective tissue diseases (systemic lupus erythematosus (SLE), primary Sjogren's syndrome, scleroderma, myositis) [14]. Detection of anti-CCP antibodies has been shown to have greater specificity (95–97%), with similar sensitivity to RF for the diagnosis of RA [15, 16]. More recently, anti-citrullinated protein antibodies (ACPA) have emerged as a distinctive subset of patients with RA [17]. It has been shown to be both a strong prognostic indicator for the development of RA in the preclinical stage and a predictor of the extent of joint destruction [18–20]. Seropositivity for ACPA at baseline has been associated with subsequent structural damage in the setting of more persistent synovitis. ACPA status has become an important autoantibody biomarker with both diagnostic and prognostic value.

The therapeutic armamentarium of RA includes combinations of symptomatic therapies such as nonsteroidal inflammatory drugs (NSAIDs) and corticosteroids, non-biologic disease-modifying anti-rheumatic drugs (DMARDs) including methotrexate, leflunomide, sulfasalazine, hydroxychloroquine and biological DMARDs such as tumor necrosis factor (TNF) blockers (infliximab, etanercept, adalimumab, golimumab, and certolizumab), interleukin-1 (IL-1) blockade (anakinra), IL-6 receptor blockade (tocilizumab), T cell co-stimulation blockade (abatacept), and B cell depletion (rituximab) with more in development. JAK inhibitors (tofacitinib, baricitinib) are newer small molecules used in the treatment of RA. Non-biologic and biologic DMARDs have demonstrated major effects on inflammation as well as tempering the pace of structural damage in the chronic

course of this illness. Thus patients require surgical interventions at a much later age than before these medications were introduced. Medications are, however, an important consideration in the perioperative setting, as they can complicate surgical interventions increasing the risk of postoperative infection and impairing wound healing (Chap. 27).

Connective Tissue Diseases

The most common of these conditions is systemic lupus erythematosus (SLE), a prototypical autoimmune disease driven by autoantibodies which target multiple organ systems including joints, skin, and kidneys. This condition occurs mainly in woman during their reproductive years (female to male ratio of 10:1) and disproportionately affects minorities, more commonly affecting African Americans, Asians, and Latinos (prevalence of 1:250–1:500), compared to Caucasians (1:2000) [21, 22]. A hallmark is the diverse clinical expression and undulating course of this condition. The relapsing-remitting pattern of disease, along with the clinical heterogeneity, makes SLE one of the challenging autoimmune disorders not only to diagnose but also to treat. The most prevalent and severe manifestation of systemic involvement is renal disease (lupus nephritis), though other important manifestations involving the musculoskeletal, cutaneous, and neurologic systems frequently arise in the course of this illness. Constitutional symptoms (fever, fatigue, malaise) are the most common presenting complaints and herald the onset of disease flares. Often, the temporal sequence of organ involvement and the severity of its course are unpredictable. While its cause remains unknown, autoantibodies directed at cell nuclei and their constituents are hallmarks of this condition and are believed important to the pathogenesis of the disease. Deposition of immune complexes on a variety of target organs results in tissue injury from inflammation, thrombosis from premature infarction of blood vessels, and/or vasculitis. Multiple mechanisms are at play, and lupus pathogenesis is complex due to nonlinear immune pathways. However, the formation of pathogenic autoantibodies as well as its defective clearance signals a dysregulated immune response with activation of the complement cascade, immune cell types (B cells, T cells), cytokines (type I interferon-α), and proteins involved in the inflammatory response. While hereditary and environmental susceptibility factors are believed important in the pathogenesis, pregnancy and certain drugs are also known disease precipitants.

Beyond the clinical complexity of diagnosis and tracking the course of illness, the challenge often becomes offering treatment modalities that strike the fine balance between immunosuppression and immune dysregulation. Corticosteroids and immunosuppressants remain the mainstay of therapy. Since their introduction in the 1950s, corticosteroids have altered the management of most rheumatic diseases and have led to gradual improvements in the morbidity and mortality of lupus patients. However, major toxicities are associated with long-term corticosteroid use, including infection, deleterious effects on bone health, and disturbances to glucose homeostasis. Thus, antimalarials (Plaquenil or hydroxychloroquine), nonsteroidal anti-inflammatory drugs (NSAIDs), azathioprine (Imuran®), methotrexate, cyclosporine, mycophenolate mofetil (CellCept®, Genentech, San Francisco, USA), and cyclophosphamide (Cytoxan®) have been utilized for their steroid-sparing and immunosuppressive effects. In addition belimumab (Benlysta®, GlaxoSmithKline, Brentford, UK), a monoclonal antibody to a soluble B-lymphocyte stimulator, is an FDA-approved medication for the treatment of autoantibody (ANA and/or dsDNA)-positive SLE patients with mild to moderate disease despite standard therapy.

As will be discussed, avascular necrosis or osteonecrosis is seen relatively commonly (4–15%) in SLE patients who have received high doses of corticosteroid therapy for serious organ involvement. Although the pathogenesis of osteonecrosis remains unclear, the final common pathway of subchondral bone destruction involves a compromise of blood flow preventing essential nutrients and normal reparative processes, leading to further osteocyte death [23]. AVN accounts for a numerically small but important indication for total joint replacement, particularly of the hip, knee, and shoulder in SLE patients (Fig. 4.7). Owing to an inherent and

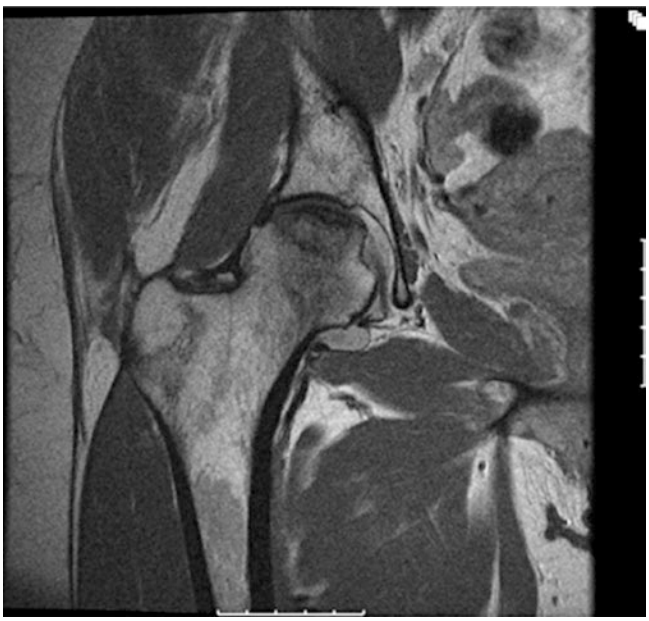

Fig. 4.7 Avascular necrosis of the hip in systemic lupus erythematosus. The R hip reveals extensive avascular necrosis involving almost the entire articular portion of the femoral head, with mild collapse of the superior femoral head. This has elicited a moderate degree of edema within the proximal right femur as well as a joint effusion of the right hip joint. Avascular necrosis also affects the greater trochanter

drug-induced immunosuppression, patients with SLE are also at increased risk for the development of septic arthritis, the acute therapy of which may require input from the orthopedic surgeon.

Autoantibodies are typically found in SLE patients and may be important for the diagnosis. Antinuclear antibodies (ANA) are a hallmark of SLE. These are antibodies directed against the cell nucleus. The ANA is positive in 95–99% of patients. Values of 2+ or greater or titers of 1:40 or greater are considered abnormal. The pattern of the ANA (e.g., speckled, diffuse, rim, centromere) can provide differential diagnostic information. Homogenous patterns are least specific, whereas rim pattern is characteristic of SLE. SLE patients may have high-titer anti-double-stranded anti-DNA antibodies. A decrease in complement level (C3 and C4) may precede the disease flare in SLE. Antibodies to extractable nuclear antigens (ENA) include Anti-Ro, Anti-La, Anti-Smith, and Anti-RNP which are often seen in SLE patients and other related disorders. For example, Anti-Ro and Anti-La are specifically seen in Sjogren's syndrome, whereas Anti-RNP is seen in mixed connective tissue disease. Many other laboratory tests may be abnormal in SLE and can be used in conjunction with the more specific tests for assessing disease. These include a low white blood count (usually with neutropenia and lymphopenia), anemia (sometimes an autoimmune hemolytic anemia with positive Coombs), thrombocytopenia, and elevated partial thromboplastin time (PTT).

Antiphospholipid syndrome is a systemic connective tissue disorder characterized by venous or arterial thrombosis and/or pregnancy morbidity. It can occur as a primary condition or in the presence of SLE or other systemic autoimmune disease. It is characterized by antiphospholipid antibodies and thrombocytopenia. Patients with these syndromes may present with ischemia, necrosis, and gangrene of the toes. Many patients with antiphospholipid syndrome present with avascular necrosis of joints. Standard antiphospholipid antibodies include the lupus anticoagulant, anti-cardiolipin antibodies, beta-2 glycoprotein. Treatment with anticoagulation is usually indicated. In the perioperative setting, patients with antiphospholipid syndrome need to be carefully monitored as the risk of thrombosis can be extremely high during these times.

Another important condition of the connective tissue is that commonly known as systemic sclerosis (scleroderma). Scleroderma exits in two major and distinct forms: localized scleroderma (LSc), which is confined to the skin and subcutaneous tissues, and systemic sclerosis (SSc), which almost always has internal organ involvement but may be limited or diffuse in its cutaneous distribution. Limited disease is defined as skin thickening that affects the distal extremities below the elbows and/or below the knees and to a lesser extent involves the face and neck, whereas diffuse cutaneous disease refers to extensive skin sclerosis affecting the proximal limbs, trunk, face, and neck regions. Rarely, systemic sclerosis can also present as *SSc sine scleroderma* with the typical vascular and fibrotic features of systemic disease but without cutaneous involvement.

Localized scleroderma, an entity that is distinct from *limited* scleroderma, includes dermatologic conditions such as morphea (circumscribed patches of thickened skin), linear scleroderma, pansclerotic morphea, or mixed scleroderma; rarely are there extracutaneous manifestations. Localized and limited scleroderma should be thought of as two distinct diseases with different clinical manifestations and prognosis (Fig. 4.8). In limited cutaneous sclerosis, formerly termed as CREST syndrome (*c*alcinosis of the digits, *R*aynaud's phenomenon, *e*sophageal dysmotility, *s*clerodactyly, and *t*elangiectasia), patients generally have prominent vasculopathic phenotype. One of the most characteristic clinical manifestations of vascular dysfunction is Raynaud's phenomenon, which is due to arterial vasoconstriction in the digits precipitated by cold or stress, manifested by the triphasic color

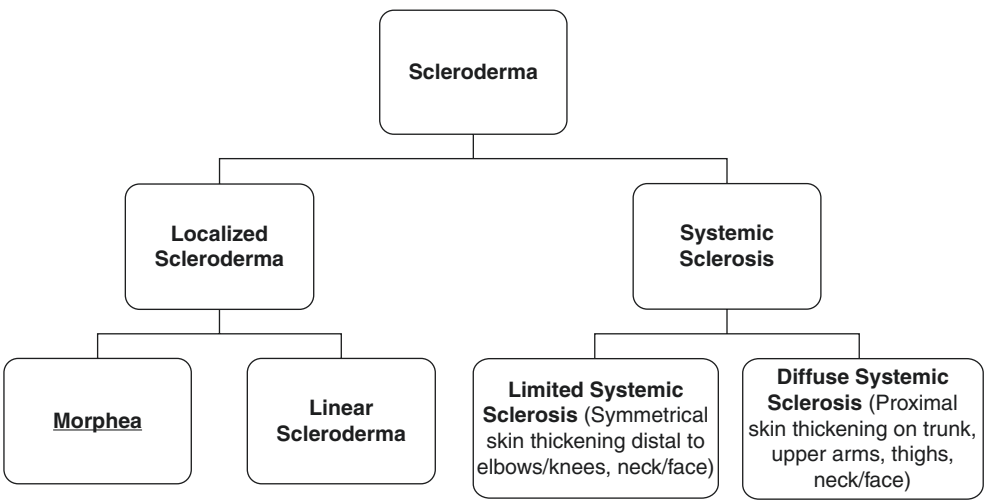

Fig. 4.8 Schematic diagram for classification of scleroderma

changes (white (pallor) → blue (acrocyanosis) → red (reperfusion hyperemia)). Abnormal nailfold capillaroscopy with scleroderma pattern is common. Pulmonary vascular disease, primarily pulmonary arterial hypertension, is more commonly seen in limited cutaneous disease, affecting up to 40% of patients. In systemic sclerosis, clinical manifestations arise as a consequence of an obstructive vasculopathy involving the small vessels, the pathological accumulation of collagen in the skin and other organ systems resulting in fibrosis, and autoimmunity as evidenced by a number of associated autoantibodies. Often a severely debilitating disease, pulmonary parenchymal disease (interstitial fibrosis) has become the most common form of death for such patients [24]. Laboratory tests often help in the diagnosis. Nucleolar and speckled pattern ANA is common in scleroderma and CREST. Anti-DNA topoisomerase I (Scl-70) antibodies, anticentromere antibody, and antibodies to RNA polymerase III may be found in patients with scleroderma. There is no effective treatment for this disorder. An important complication of this condition is the ischemic digit, usually the finger, due to an obliterative vasculopathy and vasospasm in which the caliber of blood vessels narrows and irreversible tissue loss may ensue. Chronic ischemia may lead to digital ulcers, gangrene, tapering of fingers due atrophy of underlying soft tissue, and skin changes referred to as sclerodactyly (localized thickening and tightness of the digit). A consequence of the vascular obstructive and vasospastic elements of this disease, SSc manifestations in the hand may require the participation of a hand surgeon experienced in microsurgical revascularization, digital arterial reconstruction to improve digital vascular perfusion, and peripheral sympathectomy to relieve pain. There also may be a role of surgery for advanced SSc affecting the hand, in which chronic ischemia and fibrosis may lead to atrophy and contractures of the digits, nail deformities, and calcinosis (Fig. 4.9a, b); however, surgical benefits should be balanced with risks of impaired wound

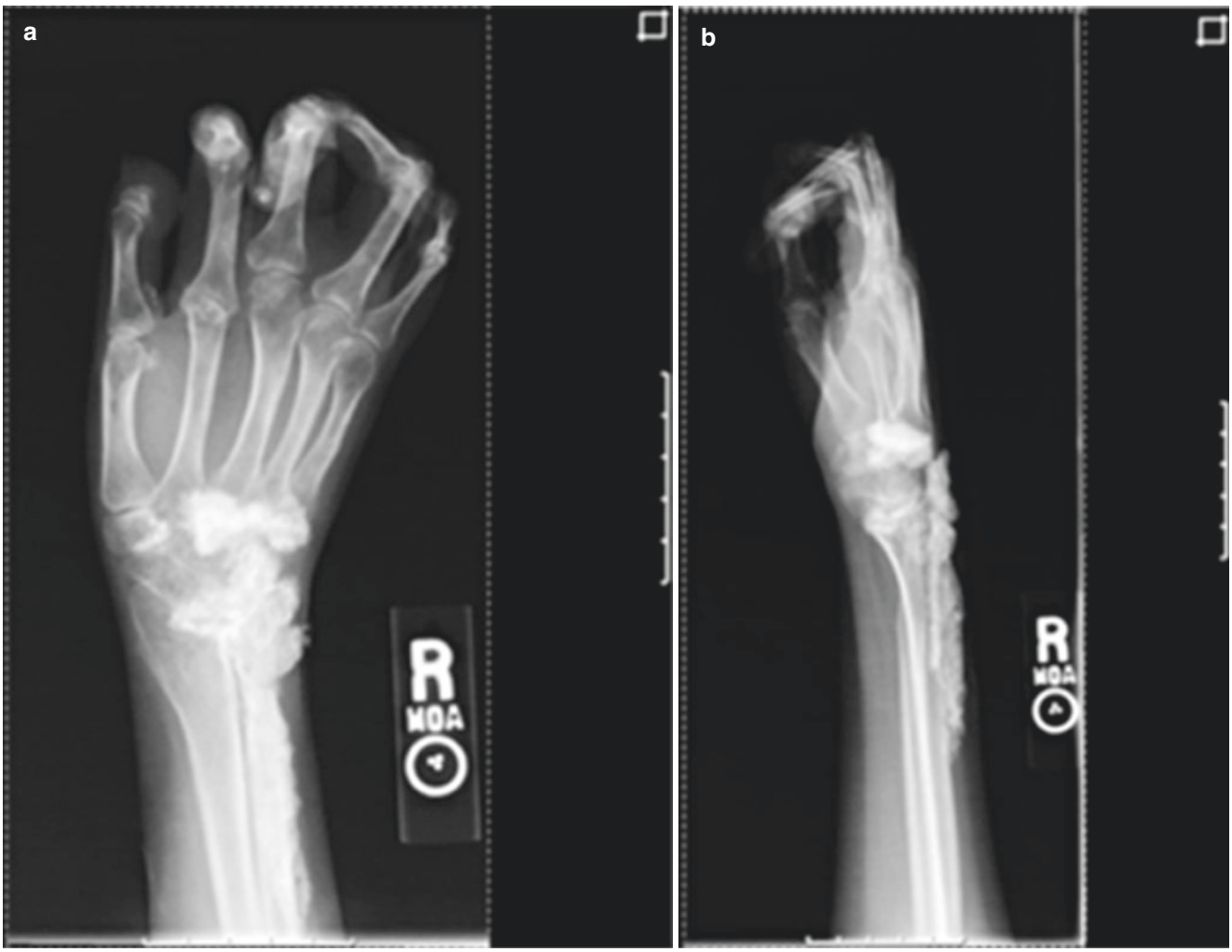

Fig. 4.9 (**a**) Calcinosis and contracture in scleroderma. (**b**) There are flexion contractures of the PIP joints bilaterally. There are soft tissue calcifications around the wrists, hands, and distal forearms bilaterally. There is acroosteolysis with loss of the terminal tufts of distal phalanges at multiple fingers

healing and the progressive course of SSc [25]. Important perioperative surveillance/screening of pulmonary disease (pulmonary arterial hypertension and/or pulmonary fibrosis) is imperative in SSc patients, especially if dyspnea is present.

A less common but important form of the connective tissue disease includes the inflammatory diseases of the muscle—dermatomyositis (DM) and polymyositis (PM). These represent another heterogeneous group of disorders, and they share the clinical features of a progressive skeletal muscle weakness and fatigue and a decrease in endurance. Disease-specific autoantibodies are also frequently found, but ultimately the diagnosis is made by muscle biopsy that demonstrates an inflammatory infiltrate. Treatment includes corticosteroids, IVIG, and immunosuppressive therapy with medication such as methotrexate and azathioprine. These diseases rarely require orthopedic intervention.

Spondyloarthritis

Spondyloarthritis (SpA) comprises a group of inflammatory disorders with overlapping clinical manifestations and a shared genetic marker (HLA-B27). The most distinguished clinical features are inflammation of axial joints (especially sacroiliac joints), asymmetric oligoarthritis, dactylitis, and enthesitis. Axial spondyloarthritis (axSpA) is a potentially disabling inflammatory arthritis of the spine, usually presenting as chronic back pain, typically before the age of 45. Patients with axSpA can be classified as having either of two subtypes of axSpA: ankylosing spondylitis (AS) or nonradiographic axSpA (nr-axSpA). AS is the prototypical SpA, but other disorders such as nr-axSpA, peripheral SpA, psoriatic arthritis (PsA), the enteropathic arthropathies, and reactive arthritis are now categorized as SpA [26]. Patients who present with clinical features suggestive, but not diagnostic, of SpA are labeled as "undifferentiated" spondyloarthritis. In contrast, those with well-defined clinical features have been referred to in the past as "seronegative" spondyloarthropathy. This designation implies the genetic, clinical, and pathophysiologic characteristics of these conditions while making reference to the absence of rheumatoid factor.

The first distinguishing feature of SpA is the presence of enthesitis, an inflammation of the bony insertion points of tendons, ligaments, or the joint capsule. Enthesitis is responsible for the multiple spinal and peripheral manifestations characteristic of this class of rheumatic conditions in which pain, stiffness, and restriction develop at sacroiliac and other spinal joints. Extraspinal enthesitis commonly affects the Achilles tendon insertions to the calcaneus and plantar fascia. A second trademark of these conditions is the presence of axial arthritis (i.e., sacroiliitis and spondylitis). Inflammatory synovitis and capsular enthesitis at the sacroiliac joints result in sacroiliitis; similarly inflammation of the entheses associated with paraspinal ligaments ultimately leads to spondylitis. Such involvement also accounts for the involvement of the intervertebral disks, symphysis pubis, and manubrioclavicular and sternoclavicular joints. These conditions are brought to their fullest expression with the addition of peripheral joint involvement, an uncommon feature in AS but commonly seen in PsA or reactive arthritis. Various patterns are commonly seen and vary according to the associated disease process. For instance, in AS, the shoulder and hips are most frequently involved. In contrast, an asymmetric lower extremity oligoarthritis (knee, ankle) is more commonly seen in reactive arthritis, while distal interphalangeal joint disease usually denotes PsA. An important feature of the SpAs is the "sausage" digit or dactylitis, an inflammatory process involving a small joint synovitis combined with an enthesitis of the tendon sheaths, insertions, and various other supporting tissues of the digit (fingers or toes). Combined, these processes produce the sausage-like swelling, a finding virtually pathognomonic of SpA. More than 90% of patients with ankylosing spondylitis (AS) and 50–70% of patients with other forms of SpA are positive for human leukocyte antigen (HLA)-B27. Acute phase reactants may also be elevated in these patients. The background prevalence of HLA-B27 is 6–10% in Caucasians, and only a small minority of HLA-B27 patients ever experience clinical manifestations, which makes the test of limited use.

As the prototypical disease among SpA, the symptoms of AS usually begin in the third or fourth decade of life with the gradual onset of inflammatory back pain. It predominantly affects men at much higher frequency than women (ratio of 9:1). Signs and symptoms of spinal involvement predominate, and the inflammatory (as opposed to mechanical) nature of the condition is suggested by a number of features: age <40 years, insidious onset, duration of <3 months, marked morning stiffness, and improvement with activity. Patients often complain of back pain at nighttime. Sacroiliitis, a common initial feature, presents as pain in buttocks which may radiate down the legs and/or hip pain. In a minority of patients, peripheral oligoarthritis and enthesitis accompany the axial involvement. Concurrent constitutional features of fatigue, weight loss, and depression often may be present. Progressive involvement of the entire spine occurs over years, resulting in spinal pain, stiffness, and severe restriction of the spine (Fig. 4.10). Family history often reveals others with early-onset back pain or inflammatory problems in the eye (uveitis, iritis). Diagnosis of AS should be predominately based on the clinical presentation of usually a young man (before the age of 40 years) who presents with chronic inflammatory back pain.

While the magnetic resonance imaging (MRI) has greatly facilitated diagnosis in SpA, various criteria have been devel-

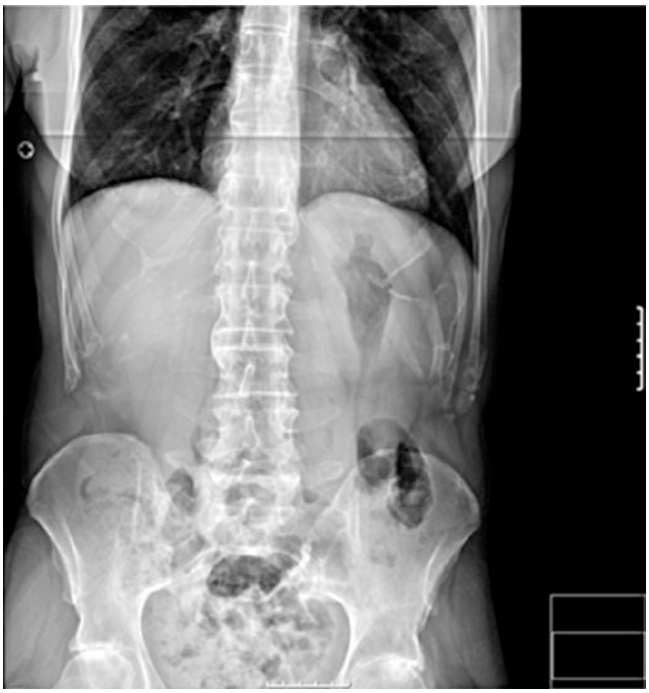

Fig. 4.10 Spinal radiograph in severe ankylosing spondylitis. There is complete fusion of the sacroiliac joints bilaterally and axial joint space narrowing of both hip joints. In the spine, bridging syndesmophytes are noted focally at L2–L3 on the *right* as well as T10–T11 on the *right* and T9–T10 on the *left*

oped both for diagnosis and for classification purposes in research and clinical trials. The New York criteria of 1968, later modified (1984), were the first such systems though have been largely replaced by the criteria described by newer criteria like the Assessment of SpondyloArthritis international Society (ASAS) that outline important clinical and radiographic features; further classifications for the peripheral forms of these diseases have also been developed (Fig. 4.11a, b) [26–31]. However, all of these classifications have low sensitivity in detecting early disease.

Patients with AS exhibit radiographic abnormalities consistent with sacroiliitis, but such findings are absent or minimal on plain radiography in nonradiographic axial spondyloarthritis (nr-axSpA). The diagnosis is supported by evidence of active inflammation of the sacroiliac joints on MRI, by a combination of other clinical findings, or both. Peripheral spondyloarthritis is the term used to describe patients with features of SpA whose symptoms and findings are predominantly peripheral.

In contrast, patients with psoriatic arthritis are also often young, but rather than spinal disease, the more typical presentation is that of an asymmetric oligoarthritis in conjunction with other characteristic features such as destructive DIP involvement, nail changes, sausage digits, arthritis mutilans, and the aforementioned peripheral enthesopathy (often the Achilles tendon or plantar fasciitis). For those that do have spondyloarthritis of PsA, the asymmetric involvement of sacroiliitis can distinguish that from the spondyloarthritis of AS, which classically affects both sacroiliac joints. Also, approximately a third of patients with psoriasis will develop PsA; the majority of patients develop psoriasis years prior to inflammatory musculoskeletal features; however, there is a group of patients (15–20%) in whom the joint disease precedes the skin disease [32]. PsA can develop in people who have any level severity of psoriatic skin disease from mild to very severe. With respect to the enteropathic disease entities, this form of inflammatory arthritis develops in patients with Crohn's disease, ulcerative colitis, or microscopic colitis. Sacroiliitis is common, and the peripheral joint arthritis tends to take the form of a large joint inflammatory process that follows the clinical activity of the underlying gastrointestinal disease. The pattern of arthritis is variable; it is commonly asymmetric but can present in a migratory or additive fashion and tends to be non-erosive. Arthritis associated with Crohn's disease and with ulcerative colitis will have negative stool and synovial fluid cultures. Intestinal biopsy and histopathology are helpful in confirming clinical suspicions. Anti-*Saccharomyces cerevisiae* antibodies (ASCAs) may be positive in ulcerative and microscopic colitis.

Lastly, there is reactive arthritis formerly known as "Reiter's syndrome." This is the clinical presentation of inflammatory arthritis coupled with extra-articular features seen in susceptible individuals following a genitourinary or gastrointestinal infection. Such individuals develop a seronegative, inflammatory arthritis arising weeks after the antecedent infection accompanied by ocular (conjunctivitis, uveitis), mucocutaneous (oral ulcers, balanitis, keratoderma blennorrhagicum), gastrointestinal (dysenteric), and genitourinary manifestations (urethritis, cervicitis). Infectious agents most often implicated include *Chlamydia*, *Salmonella*, *Campylobacter*, *Yersinia*, and *Shigella* species. These organisms are rarely cultured from the joint fluid or synovial tissue, hence the designation *reactive*. The peripheral joint involvement is usually an asymmetric lower extremity oligoarthritis, though, as with the other spondyloarthritis, sausage digits (dactylitis) are also a common feature. Axial involvement is uncommon and distinguishable from AS by its predominate asymmetric pattern of sacroiliitis and paramarginal syndesmophytes. Lastly, patients may present with features suggestive (seronegative oligoarthritis and enthesitis) but not diagnostic of these conditions. In such patients the diagnostic designation is that of an undifferentiated spondyloarthritis.

Once difficult to treat with nonsteroidal anti-inflammatory drugs, new biologic therapies such as tumor necrosis factor (TNF) inhibitors have markedly improved the clinical course and symptomatic experience of patients suffering with these conditions. Nonetheless, given the peripheral joint involvement seen in these conditions, patients who suffer from these conditions ultimately may require total joint arthroplasty.

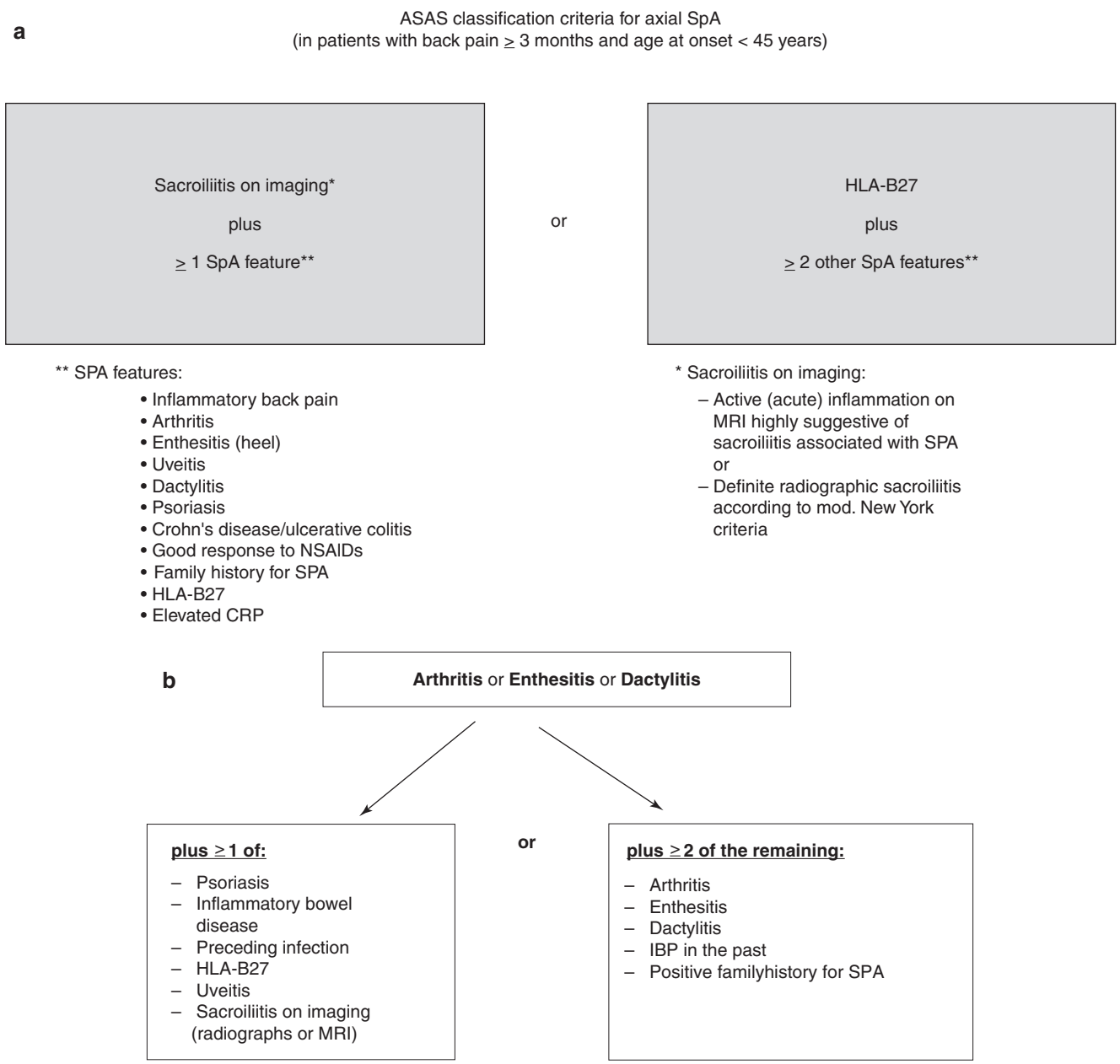

Fig. 4.11 (**a**, **b**) Criteria for diagnosing ankylosing spondylitis. Sensitivity 82.9%, specificity 84.4%; n = 649 patients with chronic back pain and age at onset <45 years. Imaging arm (sacroiliitis) alone has a sensitivity of 66.2% and a specificity of 97.3%. ∗∗Note: Elevated CRP is considered a SpA feature in the context of chronic back pain. (**a** Used with permission of BMJ Publishing Group LTD from Rudwaleit et al. [31]; **b** Used with permission of BMJ Publishing Group LTD from Rudwaleit et al. [26])

Vasculitides

The term vasculitis refers to disease conditions that involve inflammation of the blood vessels with resultant tissue necrosis and organ failure. The spectrum of disease is broad with overlapping features. While its classification systems had historically relied on eponyms, it is now categorized according to the size of the involved blood vessels. Polymyalgia rheumatica and temporal arteritis are amongst the best known examples, but also included are such conditions as polyarteritis nodosa, granulomatosis with polyangiitis (formerly known as Wegener's granulomatosis), microscopic polyangiitis, eosinophilic granulomatosis with polyangiitis (formerly known as Churg-Strauss syndrome), and cryoglobulinemic vasculitis to name a few. Often, small-vessel vasculitis will present as a rash or palpable purpura on the lower extremities and is often referred to as leukocytoclastic vasculitis. Patients often present with foot drop.

Immunologic causes of vasculitis often have characteristic laboratory findings, e.g., antineutrophil cytoplasmic antibodies (ANCA) or the presence of cryoglobulins. Acute phase reactants are usually high in these conditions. Treatment paradigms rely on corticosteroids and immunosuppressants. Orthopedic intervention is rarely needed in the course of these conditions.

Metabolic Bone Disease

Osteoporosis is a widely recognized disorder of skeletal muscle characterized by low bone mass and microarchitectural deterioration of bone, increasing its fragility and susceptibility to fracture. Pathophysiologically comprised of a heterogeneous group of disorders, osteoporosis is characterized by a net loss of bone (bone resorption activity dominating over bone formation activity) resulting in a decrease in the overall density of mineralized bone (Fig. 4.12). Osteoporotic fractures, which result from the inability of the bone to absorb a traumatic load, may have devastating consequences for patients and with an aging population have become so common as to constitute a threat to public health. Owing to the causal association between this condition and fracture (wrist, hip, spine) and the importance of bone quality in osseous healing, it is one of the most important rheumatic diseases now encountered on orthopedic services. It is important to analyze the laboratory markers like serum calcium, phosphate, magnesium, vitamin D, serum potassium, creatinine, and parathyroid and thyroid hormones when making the diagnosis and treating osteoporosis.

The aim of osteoporotic screening and treatment is to prevent fractures. Dual X-ray absorptiometry (DXA) is the primary diagnostic tool for the detection of osteoporosis. Using population standards, the World Health Organization (WHO) defines osteoporosis as a bone density measurement of the spine that is >2.5 standard deviations below the mean of the standard for a 35-year-old population in the appropriate gender. Osteopenia is defined as a T score between 1.0 and 2.5 standard deviations the bone density of a standard 35-year-old population. Additionally, the Z score provides an evaluation of bone density as it relates to age-matched controls. While bone density is a primary indicator of bone quality, there are other structural and material factors, such as bone macro- and microarchitecture, degree of mineralization and micro-damage accumulation, and bone turnover that influence overall bone quality [33]. Indeed in the orthopedic surgical setting, its implications extend to such considerations as the achievement of bony fusion after spinal surgery as well as the anticipated longevity of total joint replacement, subjects addressed in Chap. 31.

Crystal-Induced Arthropathies

Owing to fluid shifts and dehydration, gout (uric acid) and pseudo-gout (Ca^{2+} pyrophosphate) deposition in peripheral joints occurs frequently after surgery. As such, they are com-

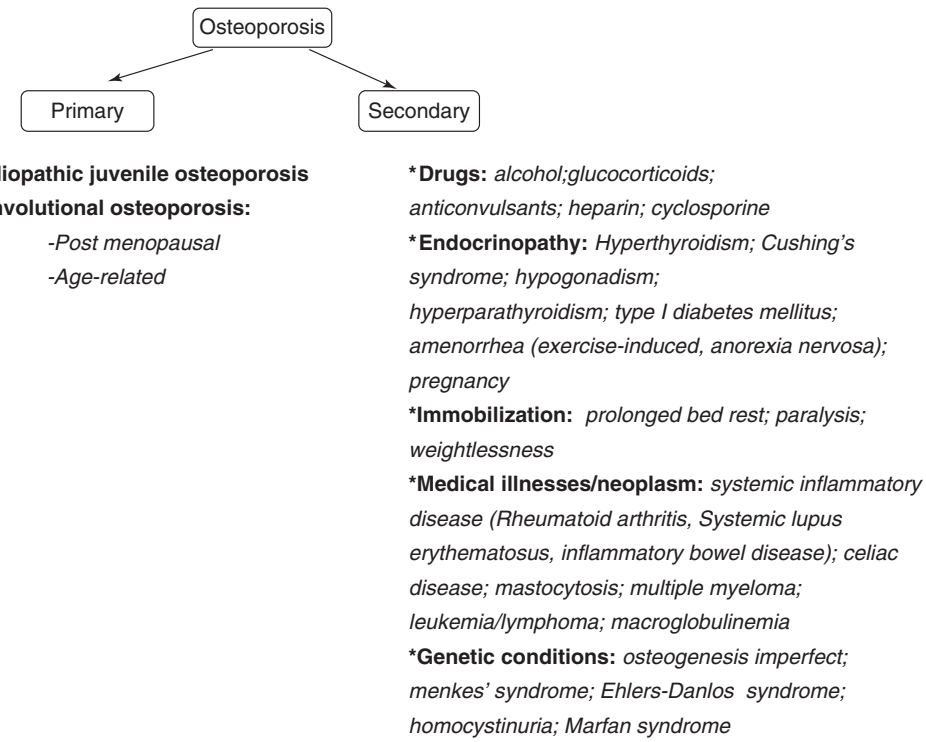

Fig. 4.12 Common causes of osteoporosis

mon management problems in the postoperative period. The archetypal presentation of these conditions is well known to clinicians taking the form of the sudden onset of severe pain, swelling, and erythema, usually of a single joint, and in approximately 50% of cases, it affects the first metatarsophalangeal joint (podagra) [34]. Other joints are not uncommon; however, the tarsometatarsal joint and ankle are frequent sites as are the knee and wrist. The latter are frequently seen in Ca^{2+} pyrophosphate crystal deposition (CPPD). Diagnosis is premised on the demonstration of pathognomonic crystals within the synovial fluid as seen via polarized light microscopy; that is, the negatively strongly birefringent, needle-shaped monosodium urate crystal in the case of gout versus the positively weakly birefringent, rhomboid crystal of CPPD (Fig. 4.13a, b). Patients with gout often have an increased uric acid level in the serum. In the postoperative setting, treatment involves the oral administration of nonsteroidal anti-inflammatory drugs, short courses of corticosteroids (or ACTH), or intra-articular injections of such steroids. Because of the potential for gastrointestinal side effects, oral colchicine is a less favored medication after surgery. The management of gout arising in the perioperative setting is fully reviewed in Chap. 22.

Another form of crystalline disease is calcium hydroxyapatite crystal deposition disease, a common entity best characterized as "calcific tendinitis" most frequently affecting the shoulder but also affecting other sites such as the hips, wrists, and feet. This syndrome is typically recognized by recurrent pain due to the pathologic peri- and/or intra-articular buildup of calcific material around the tendons/joints, which occurs as primary (or idiopathic) or as a secondary process due to various disease processes including renal disease, collagen vascular disease, metabolic disorders, or trauma. Hydroxyapatite crystals are small, amorphous, and nonbirefringent in polarized light, thereby making it difficult to diagnose with light microscopy; diagnosis is made on the basis of radiographic findings of calcium deposits in the typical periarticular and tendinous sites and concomitant clinical symptoms (Fig. 4.14). Rarely requiring surgical intervention, treatment of hydroxyapatite deposition disease involves conservative measures, such as nonsteroidal anti-inflammatory medications (NSAIDs), intra-articular steroid injections, and physical therapy.

Infectious Arthritis

Invasion of a joint by pyogenic bacteria is responsible for rapidly progressive joint destruction, osteomyelitis, and potentially systemic spread of the infection. The majority of such infections arise from hematogenous spread of offending bacteria to the affected joint(s). Predisposing factors include IV drug use, indwelling catheters, the use of immunosuppressive medication, and a host of disease processes that suppress immunity. Important examples of the latter include diabetes mellitus, chronic inflammatory arthritis, HIV infection, and alcoholism, to name a few.

The major pathogens are the gram-positive cocci (usually staphylococcal species) accounting for >75% of cases. *Staphylococcus aureus* is the most common offending agent, followed by streptococci and pneumococci; *Staphylococcus epidermidis* is often seen in the setting of prosthetic joint infection, rarely arising in the native joint. Gram-negative organisms, though a much less common cause of septic arthritis, are more often encountered in intravenous drug abusers. Associated

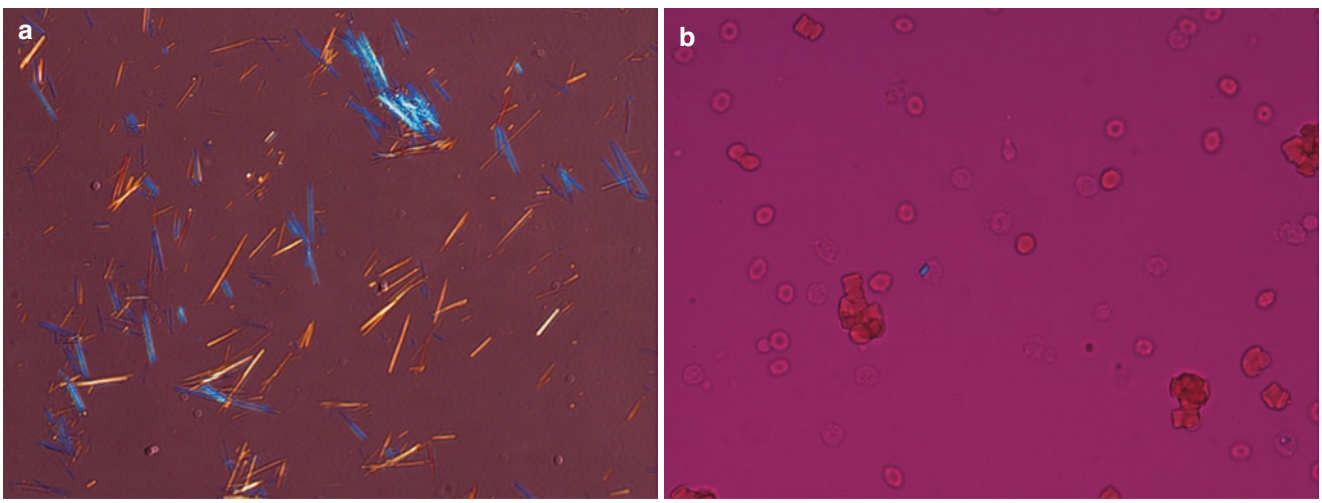

Fig. 4.13 (**a**) Gout: monosodium urate crystals. Strongly negative birefringent, needle-shaped crystals aspirate from tophaceous deposit. Crystals are *yellow* when parallel (*blue* when perpendicular) to the long axis of the first-order red compensator on polarized light microscopy consistent with gout. (**b**) Pseudo-gout: calcium pyrophosphate dehydrate (CPPD) crystals. Weakly positive birefringent, rhomboid-shaped or polymorphic crystals aspirated from joint of a patient with pseudo-gout. Crystals are typically *blue* when parallel (*yellow* when perpendicular) to the long axis of the first-order red compensator on polarized light microscopy consistent with pseudo-gout

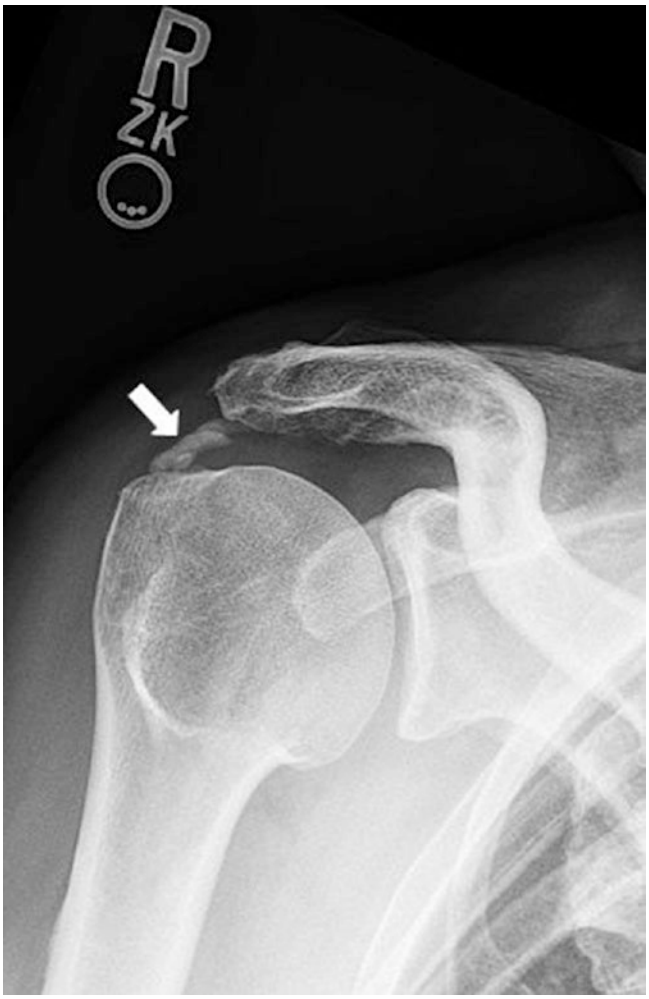

Fig. 4.14 Calcific tendonitis of shoulder. Amorphous calcific deposit on supraspinatus tendon near its insertion site at the greater tuberosity

with a purulent joint fluid (WBC >50,000, predominately granulocytes), a definitive diagnosis requires the demonstration of bacteria in the joint fluid. Antibiotic therapy logically follows from culture of the synovial fluid. Prompt diagnosis and treatment is vital in order to achieve optimal recovery. Tuberculosis has extrapulmonary manifestations which may affect joints and is common in endemic countries as well as in immunosuppressed population [35]. Removal of the prosthesis is often required followed by a course (6 weeks) of intravenous antibiotic therapy and ultimately reimplantation.

Another important infectious agent affecting the joints is the spirochete *Borreliella* causing Lyme disease. Lyme disease is caused by a tick-borne virus which often affects the knee joints. The diagnosis of Lyme disease is based primarily on the clinical history (e.g., erythema migrans, cardiac, neurologic joint), exposure to the tick vector in an endemic area, and confirmation with lab testing. If Lyme disease is suspected, a screening test is performed with ELISA followed by a confirmatory Western blot test. Patients need to be treated with appropriate antibiotics like doxycycline once diagnosed. These patients rarely require surgical intervention.

Sarcoidosis

Sarcoidosis is a disorder of unknown etiology, characterized pathologically by presence of non-caseating granulomas in affected organs. It typically affects younger adults with manifestations like bilateral hilar adenopathy, pulmonary radicular opacities, skin or eye lesions, as well as bone and joint manifestations. Articular manifestations of sarcoid may be the presenting feature of the disease and may present in isolation or combined with the other clinical manifestations. Clinically joint involvement is found in 14% of patients at presentation and may be seen up to 38% on follow-up [36]. Elevated levels of serum angiotensin-converting enzyme (ACE) can be detected. Acute sarcoid arthritis (Löfgren syndrome) commonly involves the ankle, whereas chronic arthritis mainly manifests with sarcoid bone lesions which are histologically granulomas. If these occur in weight-bearing joints, surgical intervention may be needed. The mainstay treatment for this remains corticosteroids.

Summary

The chronic rheumatic diseases represent a broad category of conditions that share a common feature, the destruction of cartilage and its consequences. While these conditions differ in their pathophysiology, the final common pathway is often the joint; hence, such patients frequently require orthopedic surgery. Presented herein is a short summary of the important conditions, presenting their broad range of clinical expression the purpose of which is the education of the readership. A second chapter (Chap. 12) in this book presents the clinical approach to the assessment of such patients prior to undergoing surgery.

Summary Bullet Points

- The chronic rheumatic diseases are prevalent conditions with a major impact on society and the healthcare system.
- Given their prevalence and the involvement of the joints, such patients may make up a significant proportion of an orthopedic patient population.
- The rheumatic diseases share one central feature: the destruction of joints.
- Although a disparate group of disorders, a systematic approach to the differential diagnosis of these conditions is presented.

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