

## Rheumatoid Arthritis – Disease Background

**Definition and Burden of Disease** Rheumatoid arthritis (RA) is a symmetric, inflammatory polyarthritis driven by autoimmunity, leading to joint damage, disability, and systemic complications. It affects 0.5-1% worldwide (higher in women, 3:1; peak 30-60 years), with U.S. prevalence ~1.5 million adults. Burden includes work disability (50% within 10 years if untreated), \$40B annual U.S. costs, and excess mortality (mainly CVD).

**Immunologic Basis and Joint Inflammation** Autoantibodies (RF, ACPA) target synovial antigens, activating T/B cells and macrophages. Cytokines (TNF- $\alpha$ , IL-6, IL-1) drive synovitis: hyperplasia, angiogenesis, and osteoclast activation erode cartilage/bone. Genetic (HLA-DRB1) and environmental (smoking, periodontitis) triggers initiate breach of tolerance.

## Typical Clinical Presentation & Extra-Articular Manifestations

- **Joints:** Insidious onset with MCP/PIP swelling, morning stiffness >1h; progresses to larger joints.
- **Systemic:** Fatigue, low-grade fever, weight loss.
- **Extra-articular (10-40%):** Nodules (subcutaneous), interstitial lung disease, pericarditis, scleritis, Felty's syndrome. Accelerated atherosclerosis doubles CVD risk.

**Impact on Function and Quality of Life** RA impairs daily activities (dressing, gripping), causing depression (20% prevalence) and reduced QoL. Untreated, 20-30% require joint replacements; early remission halves disability risk.

**Importance of Early Diagnosis and Treatment** 2010 ACR/EULAR criteria:  $\geq 6$  points from joint involvement (0-5), serology (RF/ACPA 0-3), duration (>6 weeks 1 pt), acute-phase reactants (1 pt). Early DMARD initiation (<3 months symptoms) prevents irreversible damage; "window of opportunity" improves outcomes.

## References

- Aletaha D, et al. 2010 Rheumatoid arthritis classification criteria. *Arthritis Rheum.* 2010 (reaffirmed 2024).
- Fraenkel L, et al. ACR Guideline for RA Treatment, 2021. *Arthritis Rheumatol.* 2021.