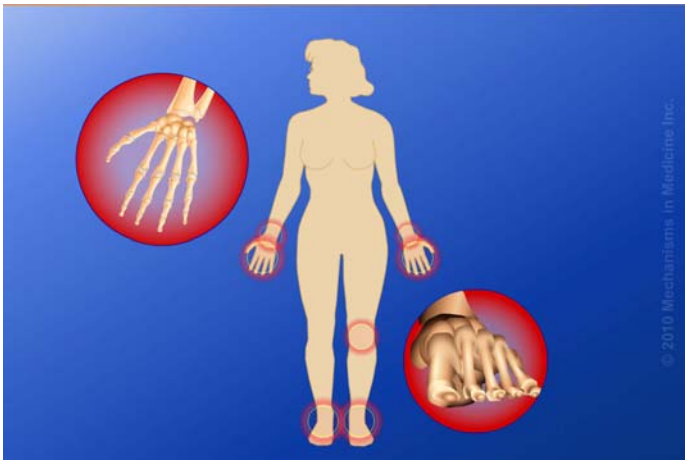
3e Recommendations in Rheumatology
Animation 2: The Pathological Processes Leading to Persistence and Destructiveness of Synovitis

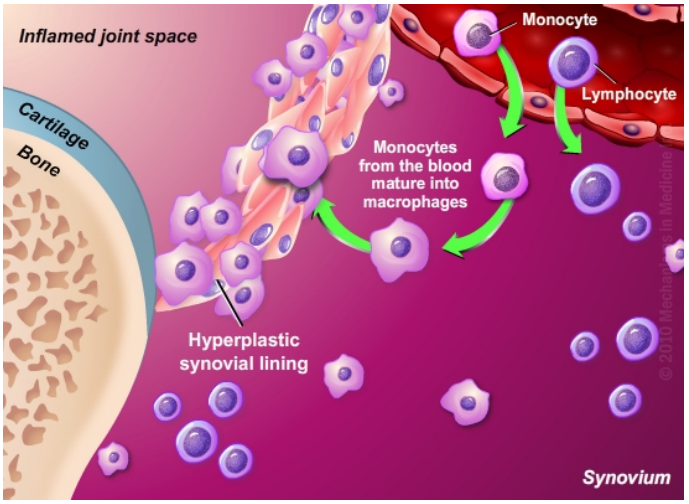
Scene 1 Notes:
Progression from UA to RA

Undifferentiated arthritis (UA) may progress to rheumatoid arthritis (RA). Depending on the characteristics of the study cohort, the literature suggests that 7% to 65% of UA cases will evolve into RA.[1(p615)] This event is most likely to occur in patients who display symmetrical polyarthritis and are anti-citrullinated protein antibody positive (ACPA) and/or rheumatoid factor (RF) positive.[1(p615)]



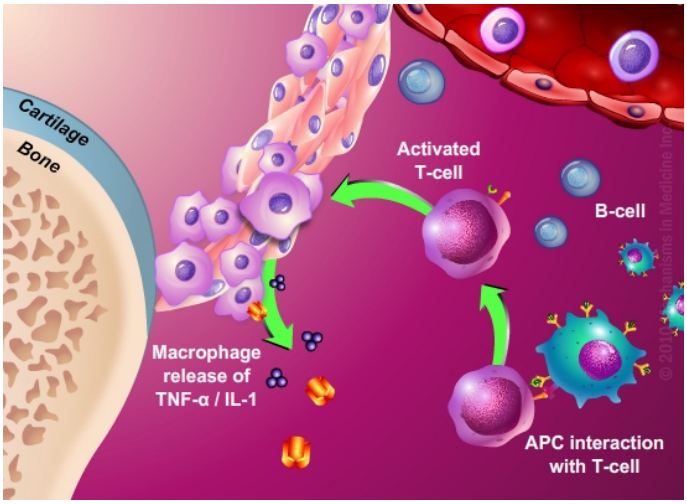
Scene 2 Notes:
Focusing on RA

In comparison to UA, patients who meet the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) criteria for RA have a greater number of joints involved and often display a symmetrical pattern of joint inflammation. This symmetrical pattern is commonly found in the joints of the hands and feet. RA patients also have a higher prevalence of radiographic erosions at the time of diagnosis and decreased functional ability as compared to UA patients.[1(p619,621)]



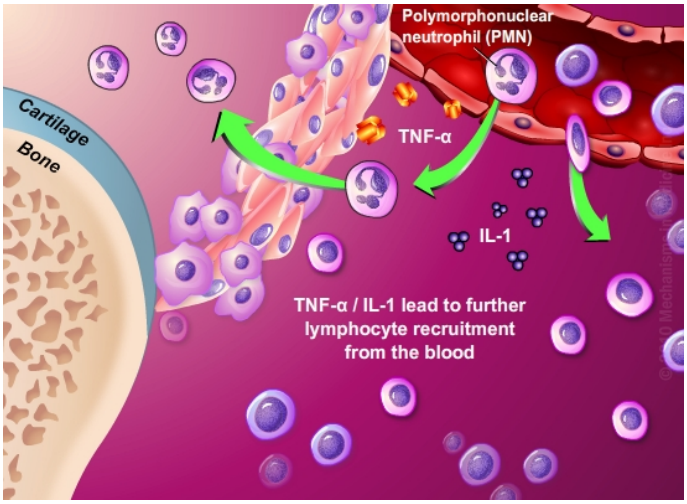
Scene 3 Notes:
At the Cellular Level: The Joint Space

The synovium of an RA affected joint is typified by the accumulation of characteristic inflammatory mediators. Monocytes and lymphocytes leave the circulation and migrate to the synovium. As the monocytes mature the number of macrophages in the synovium increases. Some macrophages remain in the synovium, further recruiting inflammatory cells; others contribute to the hyperplastic synovial lining by joining the population of macrophage-like and fibroblast-like synoviocytes.[2]



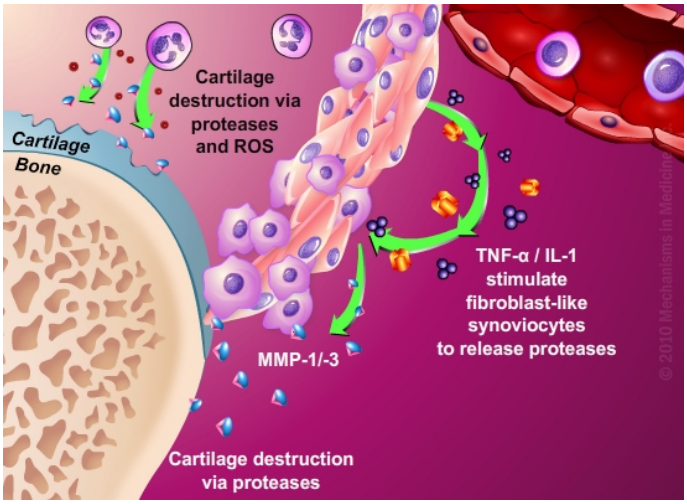
Scene 4 Notes:
The Role of APC and T-cell Interactions

Concurrently, nearby antigen-presenting cells (APCs) interact with and activate T-cells, signalling the macrophages and macrophage-like synoviocytes to release the inflammatory mediators: tumor necrosis factor alpha (TNF-α) and interleukin-1 (IL-1).[2]



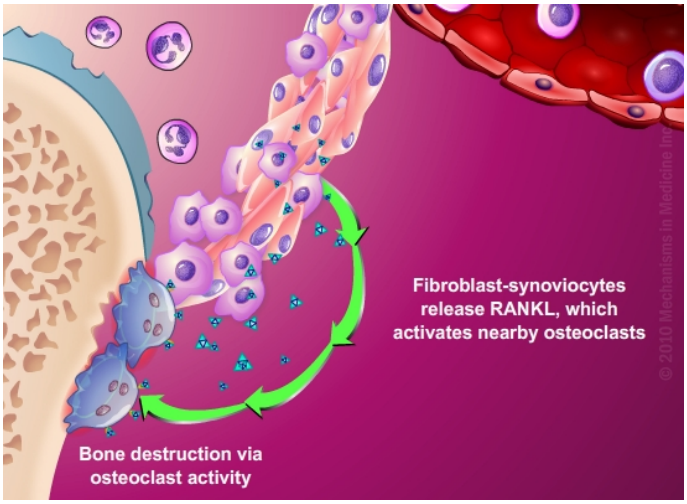
Scene 5 Notes:
Events Leading to the Destruction of Joint Cartilage and Bone

TNF-α and IL-1 signal the recruitment of additional inflammatory cells from the blood.[2] This signalling also recruits polymorphonuclear neutrophils (PMNs) from the circulation, which then proceed to migrate across the hyperplastic synovial lining and into the joint space.



Scene 6 Notes:
Events Leading to the Destruction of Joint Cartilage and Bone

The PMNs release proteases and reactive oxygen species (ROS), destroying nearby cartilage. Fibroblast-like synoviocytes, also stimulated by TNF-α and IL-1, release additional proteases such as matrix metalloprotease-1 (MMP-1) and matrix metalloprotease-3 (MMP-3), further mediating cartilage destruction.[2]



Scene 7 Notes:
Events Leading to the Destruction of Joint Cartilage and Bone

The fibroblast-like synoviocytes may also release receptor activator for nuclear factor kappa B ligand (RANKL), leading to the activation of nearby osteoclasts, which target and enzymatically destroy the bone.[2]

References:

1. Hitchon CA, Peschken CA, Shaikh S, El-Gabalawy HS. Early undifferentiated arthritis. *Rheum Dis Clin N Am*. 2005;31:605-626.

2. El-Gabalawy HS. Diagnostic tests and procedures in rheumatic disease: Synovial fluid analysis, synovial biopsy, and synovial pathology. In: Firestein GS, Budd RC, Harris ED, et al. eds. *Kelley's Textbook of Rheumatology*. 8th ed. Philadelphia, PA: Saunders/Elsevier; 2009.