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<p>Patients with rheumatic diseases often have mixed pain states, with varying degrees of nociceptive, neuropathic, and nociplastic mechanisms, which exist on a continuum. When individuals with any chronic pain have a nociplastic component to their symptoms, they are less likely to respond to treatments (eg, injections, surgery, biologics, and opioids) that work better for acute or purely nociceptive pain.</p>	
Low Back Pain in Adolescent and Geriatric Populations	149
David G. Borenstein and Federico Balagué	
<p>Spinal pain is the most common form of musculoskeletal pain. Chronic low back pain may contain nociceptive, neuropathic, and central components. Children are at risk of developing spinal pain. An increasing proportion of children develop low back pain as they become adolescents. In most adolescents, no specific diagnosis is identified. Psychological factors play a role in adolescents with back pain. Lumbar spinal stenosis causes neurogenic claudication in older patients. Magnetic resonance imaging is the best radiographic technique to detect nerve compression. Surgical decompression with or without fusion may offer greater short-term benefit but may not be significantly better than medical therapy.</p>	
Basic Mechanisms of Pain in Osteoarthritis: Experimental Observations and New Perspectives	165
Anne-Marie Malfait, Rachel E. Miller, and Richard J. Miller	
<p>The specific changes in the peripheral neuronal pathways underlying joint pain in osteoarthritis are the focus of this review. The plasticity of the nociceptive system in osteoarthritis and how this involves changes in the structural, physiologic, and genetic properties of neurons in pain pathways are discussed. The role of the neurotrophin, nerve growth factor, in these pathogenic processes is discussed. Finally, how neuronal pathways are modified by interaction with the degenerating joint tissues they innervate and with the innate immune system is considered. These extensive cellular interactions provide a substrate for identification of targets for osteoarthritis pain.</p>	

- Targeting Nerve Growth Factor for Pain Management in Osteoarthritis—Clinical Efficacy and Safety** 181
- Brett W. Dietz, Mary C. Nakamura, Matthew T. Bell, and Nancy E. Lane
- Nerve growth factor (NGF) is a neurotrophin that mediates pain sensitization in pathologic states, including osteoarthritis. In clinical trials, antibodies to NGF reduce pain and improve physical function due to osteoarthritis of the knee or hip and have a long duration of action. Rapidly progressive osteoarthritis is a dose-dependent adverse event with these agents, and additional joint safety signals, such as subchondral insufficiency fractures and increased rates of total joint replacement, are reported. The effects on pain and potential mechanisms behind these joint events both are of considerable importance in the consideration of future use of anti-NGF therapies for osteoarthritis.
- Pain in Axial Spondyloarthritis: Insights from Immunology and Brain Imaging** 197
- Ejaz M.I. Pathan and Robert D. Inman
- Inflammatory back pain is characteristic of spondyloarthritis (SpA); however, this pain may not respond to treatment with NSAIDs or biologics. Pain is multifactorial and a combination of mechanical and inflammatory factors. A growing body of literature examines the impact of emotions on pain in SpA; many patients with this condition suffer from depression and fibromyalgia. Advanced imaging techniques can investigate the interplay of various brain networks in pain perception. Animal models have helped understand the interplay between the immune and nervous systems in pain generation and have highlighted differences in pain perception between the sexes.
- The Categorization of Pain in Systemic Lupus Erythematosus** 215
- David S. Pisetsky, Amanda M. Eudy, Megan E.B. Clowse, and Jennifer L. Rogers
- Systemic lupus erythematosus is a systemic autoimmune disease that can cause severe pain and impair quality of life. Pain in lupus can arise from a variety of mechanisms and is usually assessed in terms of activity and damage. In contrast, categorization of symptoms as type 1 and type 2 manifestations encompasses a broader array of symptoms, including widespread pain, fatigue, and depression that may track together. The categorization of symptoms as type 1 and type 2 manifestations can facilitate communication between patient and provider as well as provide a framework to address more fully the complex symptoms experienced by patients.
- Why It Hurts: The Mechanisms of Pain in Rheumatoid Arthritis** 229
- Priyanka Iyer and Yvonne C. Lee
- Pain is a near-universal feature of rheumatoid arthritis, but peripheral joint inflammation may not suffice to explain the etiology of pain in all patients with rheumatoid arthritis. Inflammation in rheumatoid arthritis releases several algogens that may generate pain. Also, central nervous system processes may play a crucial role in the regulation and perpetuation of pain. Several methods for assessing pain in rheumatoid arthritis exist,

and recently the role of assessing therapeutics in treating specific etiologies of pain has gained interest.

Sexual Dimorphism in the Expression of Pain Phenotype in Preclinical Models of Rheumatoid Arthritis 245

Lauriane Delay, Gilson Gonçalves dos Santos, Elayne Vieira Dias, Tony L. Yaksh, and Maripat Corr

Rheumatoid arthritis is one of most frequent rheumatic diseases, affecting around 1% of the population worldwide. Pain impacting the quality of life for the patient with rheumatoid arthritis, is often the primary factor leading them to seek medical care. Although sex-related differences in humans and animal models of rheumatoid arthritis are described, the correlation between pain and sex in rheumatoid arthritis has only recently been directly examined. Here we review the literature and explore the mechanisms underlying the expression of the pain phenotype in females and males in preclinical models of rheumatoid arthritis.

Cannabinoids and Pain: The Highs and Lows 265

Oliver Hulland and Jessica Oswald

The medicolegal landscape of cannabis continues to change, and with ever increasing access there has been a concurrent proliferation of research seeking to understand the utility of cannabinoids in treating innumerable conditions with pain at the forefront. This article seeks to summarize clinically relevant findings in cannabinoid research to better prepare clinicians in the utility of cannabis in the treatment of pain.

Nonpharmacologic Pain Management in Inflammatory Arthritis 277

Alexander Martin, Ratnesh Chopra, and Perry M. Nicassio

This article provides an overview of nonpharmacologic options for the treatment of pain in patients with inflammatory arthritis, such as peripheral spondyloarthritis, psoriatic arthritis, ankylosing spondylitis, and rheumatoid arthritis. The experience of pain in chronic disease is a complex process influenced by multiple domains of health. The discussion focuses on the establishment of a framework for pain control that engages with factors that influence the experience of pain and explores the evidence base that supports specific modalities of nonpharmacologic pain control, such as mindfulness, cognitive behavioral therapy, exercise, massage, splinting, and heat therapy. Rheumatoid and spondyloarthritis are considered separately.