



• **FACT SHEET No. 10**

Inflammatory Pain: Rheumatoid Arthritis Pain

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Inflammatory joint pain develops when a cascade of inflammatory cytokines activate and sensitize peripheral nerve endings. Inflammatory joint pain occurs in a number of conditions. The most common is rheumatoid arthritis (RA), a systemic inflammatory disease characterized by pain and swelling in the small joints of the hands and feet.

Pathophysiology

- Pro-inflammatory cytokines recruit inflammatory cells to the synovium surrounding the joint.
- Prostaglandins and bradykinin in the synovium directly activate nerve endings.
- Cytokines, chemokines, and growth factors sensitize peripheral nerve endings.
- Glutamate, an excitatory neurotransmitter involved in pain signaling, acts on receptors in the joint and may further propagate the inflammatory cascade.
- In addition to pain caused directly by inflammation, abnormalities in central nervous system regulatory mechanisms may also lead to heightened pain in individuals with RA and other systemic inflammatory conditions.

Diagnosis

According to the 2010 American College of Rheumatology/European League Against Rheumatism RA Classification Criteria, definite RA requires synovial inflammation in ≥ 1 joint, without another diagnosis that better explains the synovitis, and a score ≥ 6 based on:



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- Number of involved joints
- Presence of rheumatoid factor or anti-cyclic citrullinated protein antibody
- Elevated erythrocyte sedimentation rate or C-reactive protein
- Duration of symptoms

These criteria are classification criteria, designed for inclusion into research studies, but they may be used as a guide for diagnosis of RA. In clinical practice, patients who do not meet these criteria may still be diagnosed with RA, depending on the specific clinical scenario.

Management

The management of pain in RA should be directed at treating inflammation, as well as pain itself. Approaches should include pharmacologic and non-pharmacologic methods.

- Methotrexate, a synthetic disease-modifying antirheumatic drug (DMARD), is the first line treatment for RA.
- Tumor necrosis factor alpha inhibitors and other biologic DMARDs are added when patients continue to have inflammatory disease activity despite treatment with synthetic DMARDs.
- Acetaminophen and NSAIDs are recommended for the treatment of persistent pain and pain associated with RA flares. A combination of acetaminophen and NSAIDs may be considered if pain is not alleviated with either medication alone.
- Some experts suggest tricyclic antidepressants or neuromodulators as adjuvant treatments for pain, directed towards central pain mechanisms. However, data supporting these recommendations are sparse.
- If pain continues despite treatment with other medications, weak opioids may be considered but should only be used for the shortest duration possible.
- When choosing medications to treat pain in RA, comorbidities (e.g., cardiovascular, gastrointestinal, renal) and concurrent medications that increase the risk of side effects should be considered.
- Psychosocial interventions (e.g., cognitive behavioral therapy) and aerobic exercise may provide added benefits to decreasing pain.

Other Inflammatory Joint Conditions

Inflammatory joint pain may be a symptom of other conditions, including:

- Crystalline arthropathies: The most common crystalline arthropathies are gout and pseudogout. Acute gout attacks are caused by an inflammatory response to monosodium urate crystals. Pseudogout is associated with an inflammatory response to calcium pyrophosphate crystals.
- Seronegative spondyloarthropathies: This group of conditions includes ankylosing spondylitis, inflammatory arthritis associated with inflammatory bowel disease, psoriatic arthritis, and reactive arthritis. They are characterized by inflammatory back pain in addition to peripheral arthritis.
- Systemic rheumatic diseases: Systemic lupus erythematosus, Sjogren's syndrome, mixed connective-tissue disease, and dermatomyositis may manifest with joint pain. These diseases can be distinguished from RA by the presence of specific systemic symptoms (e.g., rash, dry eyes, dry mouth, or muscle weakness).
- Viral polyarthritis: Common causes of viral polyarthritis include parvovirus B19, hepatitis, enterovirus, Epstein-Barr, and rubella. Inflammatory joint pain associated with viral infections is usually self-limited, lasting days to weeks.

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