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Approach to Inflammatory Arthritis for Primary Care Physicians

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Introduction

Inflammatory arthritis is a common condition encountered in primary care clinics but its diagnosis can be challenging because of the many conditions that can present with similar clinical features. As the differential diagnosis is broad, clinicians need to consider the most common entities and adopt a structured approach to establish the most likely diagnosis to help with initiating appropriate investigations and treatment.

Rheumatoid arthritis (RA), observed in 0.9% of the population, and psoriatic arthritis (PsA) affecting 0.5–2%, are the most common types of inflammatory arthritis. Ankylosing Spondylitis (AS) occurs at approximately half the frequency, with a prevalence of approximately 0.5% in the general population.[1,2]

In recent years, the term spondylarthritis (SpA) has been adopted to describe the range of inflammatory conditions with either peripheral or axial joint involvement and inflammatory arthritis. These conditions often overlap, with axial spondylarthritis (axSpA) and peripheral spondylarthritis (pSpA) co-existing in up to 70% of patients. It should also be appreciated that a subset of patients with inflammatory back symptoms may not show sacroiliac changes on X-ray, yet still meet criteria for AS. These patients are classified as having non-radiographic spondylarthritis (nrSpA). Although this term can be confusing, most of these patients usually exhibit changes in the sacroiliac joints on magnetic resonance imaging (MRI).

Additional subsets of SpA include reactive arthritis, which usually follows infections in the intestinal, urinary or genital tracts. These cases can often be treated with antibiotics with full resolution, although symptoms may persist for several months. Another subset, enteropathy arthritis, is associated with inflammatory bowel diseases, such as Crohn's disease and ulcerative colitis. Peripheral joint symptoms in enteropathy arthritis usually mirror the activity of bowel inflammation and rarely result in joint destruction. In contrast, axial involvement may follow an independent course, and the treatment may need to be distinct from that of bowel disease.

Connective tissue diseases such as systemic lupus erythematosus (SLE), myositis, and scleroderma are relatively rare conditions that can also present with inflammatory arthritis. Among these, lupus is the most frequent, affecting approximately one in a thousand individuals, with a female-to-male ratio of 10:1. Diagnosis is often guided by obvious features such as skin inflammation, muscle weakness, serositis, or involvement of major organs such as the kidneys or central nervous system. However, we often see patients who exhibit limited features of these diseases who have incomplete disease, referred to as undifferentiated connective disease. It is important to recognize these cases, as they may be associated with potentially life-threatening complications, warranting urgent or emergent referrals.

Occasionally crystal-induced arthritis, such as gout, calcium pyrophosphate deposition disease (CPPD), or hydroxyapatite, can exhibit features of symmetric or asymmetric polyarthritis, posing a challenge for clinicians. While these conditions typically present as acute monoarthritis, they may occasionally present as gout, pseudogout, and hydroxyapatite disease, but they may sometimes manifest as inflammatory arthritis involving multiple joints. Maintaining a high index of suspicion, along with bloodwork and characteristic X-ray findings, will often help make the correct diagnosis.

Lastly, the co-existence of osteoarthritis can complicate and delay the diagnosis of inflammatory arthritis. Patients with longstanding degenerative arthritis symptoms often attribute joint pain of their neck, back and peripheral joints as the natural history of osteoarthritis. As a result, elderly-onset RA or polymyalgia rheumatica (PMR) may be overlooked. A marked increase in joint complaints should prompt early blood testing to assess for elevated inflammatory markers.

History

For clinical history taking, **Box 1** provides useful questions to ask the patient. **Table 1** provides information to help distinguish between mechanical and inflammatory joint disorders.

Examination

Inspection

Table 2 provides guidance regarding joints to be assessed on examination. On inspection, affected joints will have synovial distention. Involved joints are typically not erythematous unless the underlying cause is secondary to an infection or crystal arthropathy. Of note, joint swelling can also be observed in non-inflammatory conditions such as osteoarthritis. See **Table 3** for findings that can help differentiate RA from osteoarthritis. One common example is knee swelling secondary to effusion associated with mechanical knee pathology.

See **Table 4** for information on joint involvement between RA and osteoarthritis. To evaluate the metacarpophalangeal (MCP) joints, ask the patient to make a fist and assess for the loss of "valleys" between the metacarpals. Synovitis at these joints will cause an effacement of these valleys. A similar finding may be noted at the metatarsophalangeal (MTP) joints. At the elbows, look for the loss of the sulcus between the olecranon and lateral epicondyle. At the knees, look for loss of the sulcus medial to the patella. Additionally, splaying of the toes may be observed in synovitis of the MTP joints.[3]

Palpation

Using a two-finger technique, palpate along the MCP joint lines to assess for fullness secondary to synovitis. Then, with both thumbs, palpate distal to the metacarpal heads. For the proximal interphalangeal (PIP) joints, use a four-finger technique to palpate for fullness along the joint capsule. Document which joints are tender and/or swollen, and be sure to palpate for warmth of the joints.[4]

Document findings by noting the number of tender joints and the number of swollen joints, specifying which joints are involved. For example: Tender joint count: 2 (Right second and third MCP), Swollen joint count: 1 (Right second MCP).

Questions to ask the patient:
Which joints are involved?
Is there any associated pain and or swelling?
Are there any precipitating factors such as trauma, infections, or new medications?
Is morning stiffness present, and if so, how many minutes does it typically last?
Does stiffness improve with activity?
Are there any constitutional symptoms such as fever, weight loss, or fatigue?
Are there any systemic symptoms such as rashes, mucocutaneous ulcers, chest pain, or shortness of breath?
Which therapies have been tried, including pain medication and glucocorticoids? Which of these have been effective?

Box 1. Clinical history: Questions to ask the patient; *courtesy of John P. Wade, MD, FRCPC and Ali Shams, MD, FRCPC.*

Clinical Feature	Inflammatory	Mechanical
Morning stiffness	Often more than 1 hour	Often less than 30 minutes
Activity	Can improve stiffness	May worsen pain
Rest	Can worsen stiffness	May improve pain
Systemic involvement	Can be present	Not present
Glucocorticoid responsiveness	Yes	No

Table 1. Differences between mechanical and inflammatory joint disorders; *courtesy of John P. Wade, MD, FRCPC and Ali Shams, MD, FRCPC.*

Hand: CMC, MCP, DIP and PIP	Foot: IP and MTP
Wrist	Ankle
Elbow	Knee
Shoulder	Spine: cervical, thoracic, lumbar
Hip	Temporomandibular
Sacroiliac	

Table 2. Joints to be assessed on examination; *courtesy of John P. Wade, MD, FRCPC and Ali Shams, MD, FRCPC.*

Abbreviations: CMC: carpometacarpal; **DIP:** distal interphalangeal; **IP:** interphalangeal; **MCP:** metacarpophalangeal; **MTP:** metatarsophalangeal; **PIP:** proximal interphalangeal

Finding	Rheumatoid Arthritis	Osteoarthritis
Symmetry	Often	Occasional
Synovitis	Yes	Rarely
Bone hypertrophy	No	Yes

Table 3. Findings which can help differentiate between rheumatoid arthritis and osteoarthritis; *courtesy of John P. Wade, MD, FRCPC and Ali Shams, MD, FRCPC.*

Joint	Rheumatoid Arthritis	Osteoarthritis
DIP	No	Yes
PIP	Yes	Yes
MCP	Yes	No
Wrist	Yes	No

Table 4. Joint Involvement between rheumatoid arthritis and osteoarthritis; *courtesy of John P. Wade, MD, FRCPC and Ali Shams, MD, FRCPC.*

*Of note, seronegative inflammatory arthritis, also known as PsA, can involve the DIP joints and is often asymmetric in nature making it more difficult to differentiate from osteoarthritis.

Abbreviations: DIP: distal interphalangeal; **MCP:** metacarpophalangeal; **PIP:** proximal interphalangeal

Investigations

Laboratory investigations are important in establishing a diagnosis and excluding other diseases. They may also be valuable for assessing disease activity, monitoring therapeutic response, and ensuring medication safety.

Baseline laboratory tests may include a complete blood count (CBC), c-reactive protein (CRP), urinalysis, creatinine, liver enzymes, serum protein electrophoresis (SPEP), rheumatoid factor, anti-cyclic citrullinated peptide (anti-CCP), and antinuclear antibody (ANA). It is also advisable to screen for hepatitis B, hepatitis C, and HIV at baseline, as these infections may influence treatment decisions. Genetic testing for RA and PsA is currently not useful. If the diagnosis of inflammatory back disease is suspected, testing for HLA B27 status can support the diagnosis, although its presence alone is not diagnostic. HLA B27 is present in 5–7% of the general population and in approximately 85% of patients with SpA.

Additional laboratory tests that could be considered include serum ferritin, calcium, and uric acid levels, which can help exclude diseases such as hemochromatosis and crystal-induced arthritis.

Rheumatoid factor is present in up to 5% of the general population and in up to 60–70% of patients with RA, making it neither sensitive nor specific. Anti-CCP antibodies offer greater specificity for RA. The combination of being both RF positive and anti-CCP positive greatly increases the likelihood of RA.

Currently, there are no specific blood tests for diagnosing PsA, and a normal CRP should not rule out a diagnosis as the CRP may remain in the normal range.

If a connective tissue disease such as SLE is suspected and the ANA is positive, further testing, including extractable nuclear antigen panel, anti-double-stranded DNA, and complement levels (C3, C4) are appropriate. Unfortunately, many current ANA test kits are less sensitive than earlier versions to help screen for a connective tissue disease with sensitivity falling below 90%, making diagnosis more challenging. In addition, a positive ANA result alone is not diagnostic, as up to 5% of the general population may test positive. The lack of sensitive and specific tests underscores the importance of the clinical history; clinical symptoms should drive the diagnosis, with laboratory tests serving to help confirm the diagnosis.

Imaging

X-ray imaging is often of limited value in early disease but may be performed to establish a baseline for future comparison. In cases with more longstanding symptoms, X-rays may help in confirming a correct diagnosis and evaluating whether there is advanced joint damage, which may inform decisions when surgery is a consideration.

In RA, radiographic features include symmetric joint space narrowing and characteristic joint erosions; however, these changes often take months to years to appear. X-rays of the lumbar spine and sacroiliac joints help in diagnosing SpA, though they are not sensitive in early disease.

Ultrasound is a tool that may be helpful in assessing joint swelling and inflammation, but may yield both false-positive and false-negative results. Its most useful application is in assessing the rotator cuff of the shoulder, where clinical assessment is poor. Additionally, ultrasound may help in guiding corticosteroid injections when this is a treatment consideration.

CT scanning is typically not considered useful; however, it may be highly informative when performed by an experienced radiologist using dual energy CT (DECT) technology. This imaging technique may confirm the presence of uric acid deposits in soft tissues, detect characteristic erosions, and identify CPPD.

CT scanning of the sacroiliac joints offers more sensitivity than plain radiographs in looking for changes suggestive of SpA. However, it is limited to specialized centres where the radiologists have the expertise and access to advanced imaging techniques, which helps to make an earlier diagnosis.

MRI is the most sensitive imaging technique for assessing early synovitis and joint damage but is expensive and not readily available in most communities. Studies show that artificial intelligence (AI) is as reliable as radiologists in interpreting MRI scans. As AI technology becomes more affordable and available, it will likely have an increasing role in both diagnosing and monitoring disease.

Treatment

Initial treatment for inflammatory arthritis includes nonsteroidal anti-inflammatory drugs (NSAIDs), prescribed at the lowest dose to control symptoms. Patients must be counselled on the risks associated with these medications. Gastrointestinal (GI) side effects such as dyspepsia are common, but more serious complications, including perforations, ulcers, and bleeds occur in 1–2% of patients annually. The risk of these events can be reduced by approximately 50% with the concomitant use of medications to reduce gastric acidity. It is important to note that GI bleeding may present as the first manifestation of a complication. Patients need to be educated on the safe use of these medications. Additional concerns of NSAIDs include increased blood pressure, renal dysfunction, and cardiovascular events, particularly in older adults.[5]

Topical NSAIDs offer a safer but less effective treatment for inflammatory arthritis, though they can be used as an adjuvant to therapy. Higher-concentration formulas, such as diclofenac 10–20% cream, are helpful but often require compounding by a pharmacy and are expensive.

Targeted steroid injections into the most active joints are very effective, though their benefit is limited to 1–2 months. These injections may also exert a systemic effect, and help to reduce overall inflammation.

Oral prednisone is very effective in the short term, both for helping to confirm a diagnosis of inflammatory arthritis and to treat symptoms. Unfortunately, oral prednisone is effective in the short term, but tapering can be difficult. Common early side effects include increased appetite, weight gain, poor sleep, GI complaints, and sometimes agitation. More serious long-term concerns are thinning of the skin and bruising, elevated blood glucose, elevated blood pressure, muscle weakness, serious infections, and osteoporotic fractures. If a patient responds well to prednisone, it is important to begin tapering early and introduce steroid sparing agents.

If the patient continues to experience persistent symptoms, early introduction of a disease-modifying anti-rheumatic drug (DMARD) should be considered to slow or stop inflammation and prevent joint damage. These medications take weeks to months to take effect, so they are most appropriate when a chronic inflammatory condition is likely. Their goal is to suppress or modify the immune system and prevent damage. Conventional first-line DMARDs include methotrexate, sulfasalazine, leflunomide, and hydroxychloroquine. Combination therapy with DMARDs in addition to NSAIDs is an effective approach for managing RA and PsA. Primary care physicians should feel comfortable starting these

medications prior to specialty referral, provided they are familiar with dosing and side effects. National arthritis association websites provide valuable patient information to help support informed consent by outlining both the benefits and side effects of treatment.

Methotrexate is commonly prescribed as an oral weekly dose of 15 mg. If well tolerated and disease activity persists, the dose can be increased to 25 mg weekly, administered either orally or subcutaneously. Folic acid can be co-prescribed at a dose of up to 1–5 mg daily (or 6 days per week) to minimize side effects. Monthly monitoring should include blood tests for CBC, creatinine, and liver enzymes. Women of childbearing potential must be informed that methotrexate can cause birth defects; effective contraception should be discussed, and alternate medications considered for those wanting to conceive. Leflunomide, taken orally at 10–20 mg daily, is also absolutely contraindicated during pregnancy and should be discontinued 6–24 months prior to conception. Sulfasalazine is initiated orally starting at 500 mg daily, with gradual weekly increases up to 2000–3000 mg daily. Hydroxychloroquine is a less effective agent but has fewer side effects and can be safely started at 200–400 mg orally per day. Baseline ophthalmologic testing should be arranged promptly, followed by annual eye exams after 5 years of continuous therapy.

For patients with very active disease or those who do not respond to combination therapy or DMARDs, escalation to a biologic DMARD or a targeted DMARD should be considered. These therapies are typically started by a rheumatologist; however, primary care providers should understand the rationale for their use and be aware of potential concerns, as they will be involved in ongoing patient care.

Common biologic DMARDs for RA include tumour necrosis factor (TNF) inhibitors (etanercept, adalimumab, infliximab, golimumab, certolizumab), interleukin (IL)-6 inhibitors (tocilizumab), B-cell depleting agents (rituximab), T-cell modulators (abatacept). These medications are administered either by self-injection on a weekly to monthly schedule or via intravenous infusion every month to 6 months.[6,7]

Biologic therapies for PsA and SpA may include TNF inhibitors at the same doses used for RA, as well as additional agents such as IL-17 inhibitors (secukinumab, ixekinumab, bimekizumab). Other options include IL12/23 inhibitors (ustekinumab) and IL-23 inhibitors (guselkumab risankizumab), although these latter agents are more commonly prescribed for psoriasis and inflammatory bowel disease and have limited efficacy in treating inflammatory back disease.[8-10]

In addition to injectable biologics, targeted oral therapies known as Janus kinase inhibitors (tofacitinib, baricitinib, upadacitinib) have been approved for the treatment of inflammatory arthritis. These agents are administered as daily oral tablets and are effective for a variety of inflammatory conditions.[11]

Summary

Inflammatory arthritis is commonly encountered in primary care and may present either acutely or insidiously, posing a major challenge for clinicians. A logical approach to history-taking and physical examination is important to establish the most likely differential diagnosis and guide further investigations. Joint inflammation results in pain and swelling, which over time can lead to joint destruction and poor quality of life. Early diagnosis and treatment are important to ensure that correct treatment is started. Advances in therapy have had a major impact in controlling joint inflammation thereby reducing cartilage destruction and maintaining joint function.

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