

## REVIEW ARTICLE

# Approach to Polyarthritis for the Primary Care Physician

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## KEYWORDS:

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Complaints of joint pain are commonly seen in clinical practice. Primary care physicians are frequently the first practitioners to work up these complaints. Polyarthritis can be seen in a multitude of diseases. It can be a challenging diagnostic process. In this article, we review the approach to diagnosing polyarthritis joint pain in the primary care setting. Starting with history and physical, we outline the defining characteristics of various causes of arthralgia. We discuss the use of certain laboratory studies including sedimentation rate, antinuclear antibody, and rheumatoid factor. Aspiration of synovial fluid is often required for diagnosis, and we discuss the interpretation of possible results. Primary care physicians can initiate the evaluation of polyarthralgia, and this article outlines a diagnostic approach.

## INTRODUCTION

Polyarticular joint pain is a common complaint seen in primary care practices. The differential diagnosis is extensive, thus making the diagnostic process difficult. A comprehensive history and physical exam can help point towards the more likely etiology of the complaint. The physician must first ensure that there are no symptoms pointing towards a more serious diagnosis, which may require urgent management or referral. It is then important to differentiate between true articular pain versus pain which arises from outside the joint. Distinguishing whether the arthritis has an inflammatory component can further narrow down the differential diagnosis. Inflammatory conditions will often cause synovitis with warmth and swelling, as well as prolonged morning stiffness. These conditions also cause constitutional symptoms, and patients may report other associated complaints such as rash or ocular involvement. Physical exam of a patient with osteoarthritis, a non-inflammatory condition, will often reveal osteophytes and crepitus, as opposed to an inflammatory arthritis, which will demonstrate findings of synovitis. Laboratory and imaging studies are often nonspecific, but may help rule in or rule out certain diagnoses. Much of the initial workup for polyarthritis can be done in the primary care setting using proper clinical investigation and appropriate diagnostic studies (See Figure 1).

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## PATIENT HISTORY

Although laboratory studies can shed much light on a possible diagnosis, a detailed history and physical examination remain crucial in the evaluation of polyarticular symptoms. The vast differential for polyarticular pain can be greatly narrowed using a thorough history.

### Emergencies

During the initial evaluation, the physician must first exclude any life-threatening conditions, which may present with arthritic-type symptoms. Urgent orthopedic evaluation should be considered in the setting of significant injury to a joint. A warm, swollen joint should raise concern for infection before a diagnosis of gout or pseudogout is given. While constitutional symptoms such as fever, weight change, or fatigue may indicate a systemic rheumatic disease, sepsis from infection must be ruled out. Weakness may be a sign of muscle dysfunction, such as myositis or a degenerative neuromuscular disorder. Radiculopathy must be considered in the presence of neurogenic pain. Once we have ruled out these serious diagnoses, we may further focus on the patient's symptoms.<sup>1</sup>

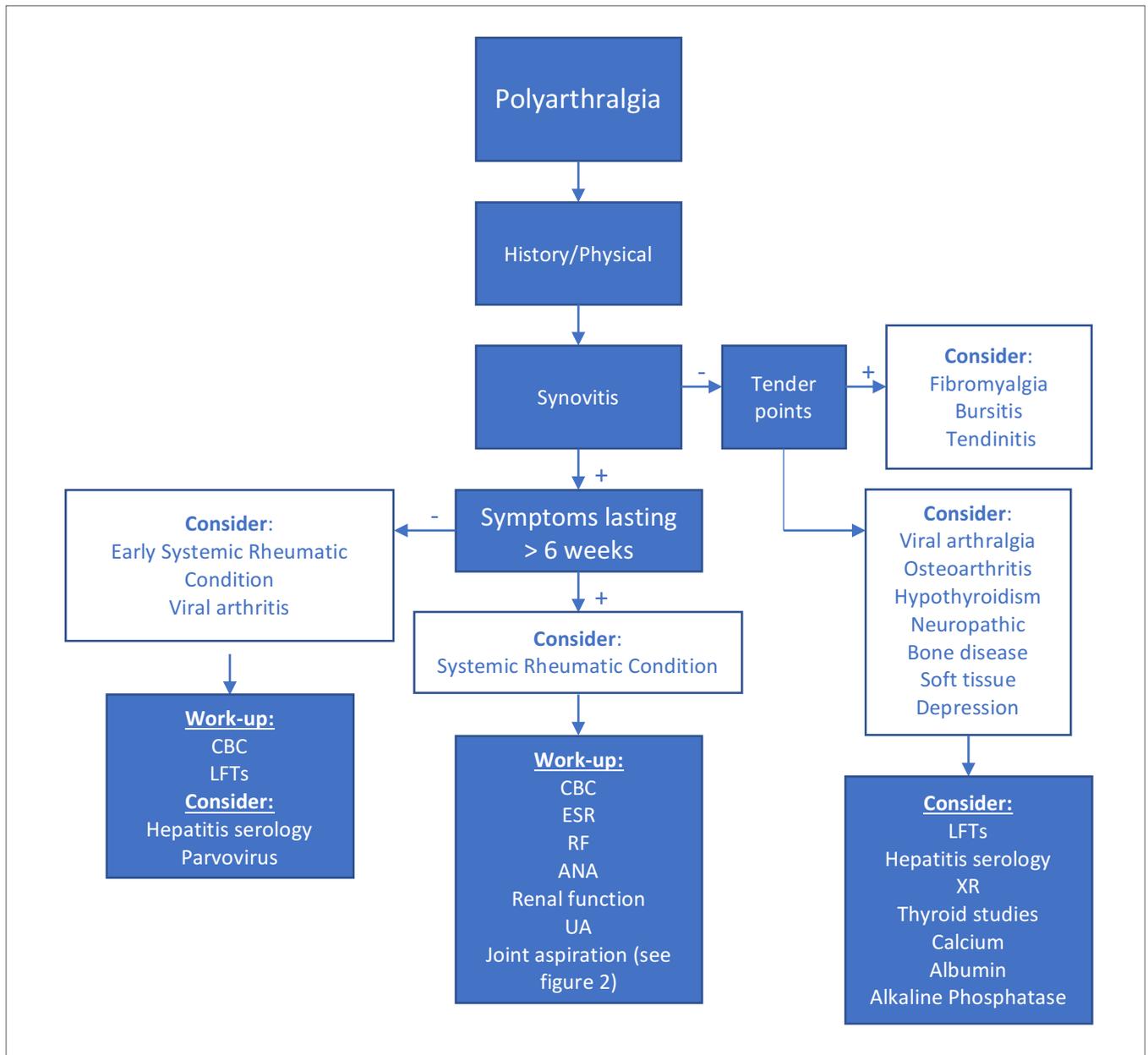
### Joint Involvement

Characterizing the joint symptoms a patient is experiencing is an important aspect of the diagnostic approach. The physician must determine whether the patient is experiencing true joint inflammation as opposed to periarticular pain as seen with tendonitis or bursitis. Usually, joint swelling will not be seen in non-arthritic conditions.<sup>2</sup> Arthritis is defined as joint inflammation alongside joint pain. This is in contrast to arthralgia, which lacks the inflammatory component. It is important to make this distinction. Markers of inflammation include surrounding erythema, warmth, tenderness, and swelling of the joint.<sup>3</sup>

The quality of pain a patient reports can help guide the physician. True articular pain would be expected to improve with rest of the joint and worsen with movement or stress. Neurogenic pain would cause feelings of

FIGURE 1:

General approach for evaluation of polyarthralgia symptoms<sup>1</sup>



numbness, burning, or a “pins and needles” sensation. This type of pain will not worsen with joint movement and is often more severe at night. Claudication, or pain from arterial insufficiency, will promptly improve with rest. Inflammatory arthritis would cause pain which persists even with rest.<sup>1,4</sup>

The timeframe of symptoms must be established. Acute symptoms persist anywhere from hours to two weeks. Symptoms lasting more than two weeks are considered chronic. Chronic symptoms may be constant or intermittent. Investigating these patterns may help identify certain triggers or associated conditions.<sup>4</sup>

Rheumatoid arthritis (RA) classically affects multiple joints in a bilateral and symmetrical pattern. Patients will present with pain, stiffness, and swelling of joints. Morning stiffness is a common complaint and often lasts more than one hour after awakening.<sup>5</sup> Other systemic rheumatic diseases, such as systemic lupus erythematosus (SLE) and polymyalgia rheumatica, may present with similar patterns. Spondyloarthropathies, including ankylosing spondylitis, reactive arthritis, psoriatic arthritis, and arthritis associated with inflammatory bowel disease are characterized by the presence of the HLA-B27 gene. Joint involvement with these conditions is typically asymmetric and commonly involves inflammation of the sacroiliac joints and spine. Enthesitis, inflammation of the insertion site of tendons or ligaments, is the hallmark of the spondyloarthropathies.<sup>6</sup>

The joints involved can provide important clues. Rheumatoid arthritis will usually affect the proximal interphalangeal joints (PIP), as well as the metacarpophalangeal joints (MCP), but will not involve the distal interphalangeal joints (DIP). This differentiates between osteoarthritis which will involve the DIP and PIP, but spares the MCP.<sup>7</sup> SLE affects similar joints as RA, however there is rarely bone destruction.<sup>2</sup> Any of these joints can be affected with psoriatic arthritis, gout, pseudogout, and sarcoid. Lyme disease differs as inflammation of the hand is not commonly seen.<sup>3</sup> Early Lyme often causes a migratory arthralgia, later progressing to arthritis of mainly large joints.<sup>8</sup> In one study, 51 percent of patients developed arthritis weeks to months after being diagnosed with Lyme disease. The majority of patients experienced knee effusions, but other large and small joints, such as temporomandibular joint, were also involved. Many patients experienced recurrent attacks, with some progressing to chronic arthritis.<sup>9</sup>

Bacterial arthritis from a nongonococcal source classically occurs in one joint, with only 10 to 19 percent of cases having polyarticular involvement. Gonococcal arthritis is typically polyarticular and may have a migratory pattern. Systemic signs such as fevers, chills, and a vesicular rash are common.<sup>8</sup>

Various viral infections may cause arthritic symptoms. An episode of polyarthritis may be the early signs of a fulminant hepatitis B infection, causing joint pain and fevers during a prodromal phase.<sup>8</sup> HIV must be considered, as early disease may cause various forms of arthralgia. Patients may experience episodes of oligoarthritis as well as symmetrical polyarthritis.<sup>2,8</sup> Parvovirus B19 may not cause the frequently classic “slapped-cheek” rash in adults. While most adults with parvovirus infection are asymptomatic, approximately 60 percent of women who are symptomatic will develop arthropathy. These patients will often complain of polyarthritis which is symmetric and affects small joints such as hands, knees, wrists, and ankles. While most see resolution of symptoms in one to three weeks, 20 percent of women will continue to have pain which could last years. In one study on parvovirus B19, 48 percent of adults studied described a symmetrical polyarthropathy. Most complained of pain and stiffness. Several women experienced recurrent episodes of joint symptoms after resolution of the infection.<sup>10</sup> Children are less likely than adults to experience parvovirus-related arthropathy. As opposed to adults, children usually have involvement of large joints in an asymmetric pattern.<sup>11</sup>

If a patient experiences joint tenderness and swelling which fully resolves, followed by recurrent attacks, crystal-induced arthritis, such as gout, must be considered. Generally, one joint is affected with each attack. The initial presentation may involve multiple joints along with fever. Episodes may last one to two weeks, while symptom-free periods could last years early on in the course<sup>2</sup> (See Table 1).

Fibromyalgia is a condition associated with arthralgia that may be confused for polyarthritis. Patients will complain of pain of the back, elbow, trochanter, medial knee, and anterior chest. This pain can be localized to specific tender points. Symptoms are often symmetric. It is often associated with stiffness which is worse in the morning.<sup>12</sup>

**TABLE 1:**  
Differential Diagnosis of Polyarthritis<sup>2,3</sup>

<b>SYSTEMIC RHEUMATIC CONDITIONS</b>	Rheumatoid arthritis Systemic lupus erythematosus Scleroderma Polymyalgia rheumatica Polymyositis Still's Disease Sjögren's syndrome Sarcoidosis
<b>INFECTIOUS</b>	Viral Bacterial (gonococcal vs nongonococcal) Other (Lyme, tuberculosis)
<b>CRYSTAL-INDUCED</b>	Gout Pseudogout
<b>SPONDYLOARTHROPATHIES</b>	Ankylosing spondylitis Psoriatic arthritis Inflammatory bowel disease Reactive arthritis Juvenile idiopathic arthritis
<b>SYSTEMIC VASCULITIS</b>	Henoch-Schönlein purpura Polyarteritis nodosa Granulomatosis with polyangiitis
<b>ENDOCRINE DISORDERS</b>	Hyperthyroidism Hypothyroidism Hyperparathyroidism
<b>OTHER</b>	Osteoarthritis Fibromyalgia Amyloidosis Malignancy

**TABLE 2:**  
Patterns of Joint Symptoms<sup>2</sup>

SYMPTOM PATTERN	DEFINITION	EXAMPLES
INTERMITTENT	Episodes of polyarthritis symptoms with complete resolution between attacks	Gout Pseudogout Reactive arthritis
MIGRATORY	Joint symptoms resolve and then reappear in different joints	Lyme disease Gonococcal arthritis
ADDITIVE	Symptoms in joints persist, with addition of further joint involvement over time	Systemic lupus erythematosus Rheumatoid arthritis Osteoarthritis

A possible sequelae to certain urogenital and enteric infections is reactive arthritis. The most common causes are *Chlamydia trachomatis*, *Salmonella*, *Shigella*, *Campylobacter*, and *Yersinia*. Patients with this condition will experience an additive polyarthritis usually affecting large joints in an asymmetric pattern. Joint symptoms typically present one or two weeks following the infection<sup>6</sup> (See Table 2).

### Extra-articular Manifestations

Many rheumatologic causes of polyarthritis will also present with constitutional and systemic signs. Fever, weight loss, and fatigue may be seen. Multisystem involvement of diseases like RA and SLE may present with rash, adenopathy, mucosal ulcers, Raynaud's, xerostomia, and keratoconjunctivitis sicca.<sup>1</sup> Psoriatic arthritis may be suspected in the setting of a history of psoriasis and the classic nail findings such as hyperkeratosis and pitting.<sup>13</sup> The spondyloarthropathies may feature ocular involvement and mucosal lesions.<sup>6</sup>

The inflammation associated with RA stretches way beyond the boundaries of the joints. Subcutaneous and pulmonary nodules may develop. Vasculitis and peripheral neuropathy are also associated with the disease. Patients may develop pericarditis with associated effusions. Some potential ocular findings include episcleritis or scleritis.<sup>7</sup>

Similarly to RA, gout can result in cutaneous nodules referred to as tophi. These crystal deposits can distort the joint space as well as cause pain. Differentiating between RA nodules and tophaceous nodules involves aspiration and analyses of the fluid.<sup>2</sup>

In addition to the synovitis seen with rheumatoid arthritis, the spondyloarthropathies also feature enthesitis. These conditions also present with spinal inflammation and dactylitis, or "sausage digits."<sup>14</sup>

Fever may be seen in conditions other than rheumatic causes. Infection must always be entertained in the setting of fever. Gout and pseudogout are also known to cause fevers during attacks. As previously mentioned, SLE may involve fever. Spiking fevers preceding joint symptoms may be a sign of Still's disease.<sup>15</sup>

Identifying certain rashes can aid in diagnosis. As discussed earlier, history of a "slapped-cheek" rash can indicate parvovirus B19. This classic rash is described as lacy, erythematous, and maculopapular in appearance.<sup>16</sup> SLE often involves a light-sensitive rash which classically involves the face but can also be seen between joints. History of a target-shaped rash can point towards a diagnosis of Lyme disease, although the rash is usually resolved prior to the onset of joint symptoms.<sup>15</sup>

### PHYSICAL EXAM

During the exam, it is important to assess joint motion, joint integrity, and exact location of pain to help determine whether a patient is experiencing a mechanical abnormality, soft tissue disease, or true joint disease. Synovitis will present with effusion, warmth, and joint pain with movement. Further analysis will be required, as noninflammatory conditions may also present with joint swelling and effusion.<sup>1,2</sup>

Soft tissue abnormalities, such as bursitis, tendinitis, or injury to a muscle will usually present in a predictable manner. Patients will usually have intact passive range of motion but will experience decreased active range of motion secondary to pain. Point tenderness

to the affected area will often be seen. Decreased active as well as passive range of motion should raise concern for synovitis or structural joint damage. Stability of the joint must be assessed, as laxity may indicate ligament damage.<sup>1</sup> Osteoarthritis should be considered if crepitation is observed without erythema or warmth.<sup>4</sup> Septic arthritis can present with a painful, warm, erythematous joint. Based on patient history, a diagnosis of crystal-induced arthritis may be more likely.<sup>8</sup>

## LABORATORY STUDIES

After a thorough history and physical, laboratory investigations should be ordered when appropriate. It is unnecessary to do further testing once a mechanical or extraarticular problem is identified. There are a variety of tests that may help further guide diagnosis.

### Erythrocyte Sedimentation Rate & C-Reactive Protein

Both erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are nonspecific markers of inflammation. They are useful in differentiating between inflammatory and noninflammatory processes. ESR can be elevated in many diseases, and is therefore not diagnostic on its own. For example, levels will be increased in the setting of rheumatic conditions, malignancy, and infection. In the acute phase of inflammation, CRP is more reliable than ESR. Non-inflammatory conditions such as diabetes, renal disease, and dysproteinemia can increase ESR, as ESR can be affected in the setting of abnormal red blood cells. While ESR is not diagnostic, an elevated ESR level alongside a classic history and physical can further support a diagnosis of rheumatic disease or other inflammatory process.<sup>1,4</sup>

### Antinuclear Antibody

Antinuclear antibody (ANA) may be useful when considering a diagnosis of SLE. It is highly unlikely a patient with negative ANA results will have a diagnosis of SLE.<sup>1</sup> Five to ten percent of the population will have positive ANA testing without a rheumatologic

TABLE 3:

Synovial Fluid Analysis<sup>3</sup>

CLASSIFICATION	WBC count	Polymorphonuclear leukocyte count	Examples
NORMAL FLUID	0-200 per mm <sup>3</sup>	<25%	
NONINFLAMMATORY	<2,000 per mm <sup>3</sup>	<25%	Osteoarthritis
INFLAMMATORY	2,000-50,000 per mm <sup>3</sup>	>75%	Rheumatoid arthritis Psoriatic arthritis Gout
SEPTIC JOINT	>50,000 per mm <sup>3</sup>	>90%	Septic arthritis Gout Reactive arthritis

diagnosis, so it is important to consider clinical presentation alongside the laboratory testing. Positive ANA without the clinical features of a rheumatic condition should not drive a diagnosis.<sup>3</sup> Although it cannot provide a definite diagnosis as discussed, the higher the ANA titer is, the more likely a patient is to have SLE.<sup>1</sup>

### Rheumatoid Factor & Anti-Citrullinated Peptide Antibodies

Rheumatoid factor (RF) is a nonspecific marker. It may be identified in not only rheumatoid arthritis, but also Sjögren's syndrome, SLE, vasculitis, and chronic infections such as hepatitis C and tuberculosis.<sup>1</sup> RF should only be ordered in the setting of moderate suspicion for rheumatoid arthritis.<sup>1</sup> The test has poor sensitivity and specificity. Approximately 20 percent of rheumatoid arthritis patients lack RF, while five to ten percent of patients without the disease will have positive rheumatoid factor.<sup>17</sup>

### Serum Uric Acid

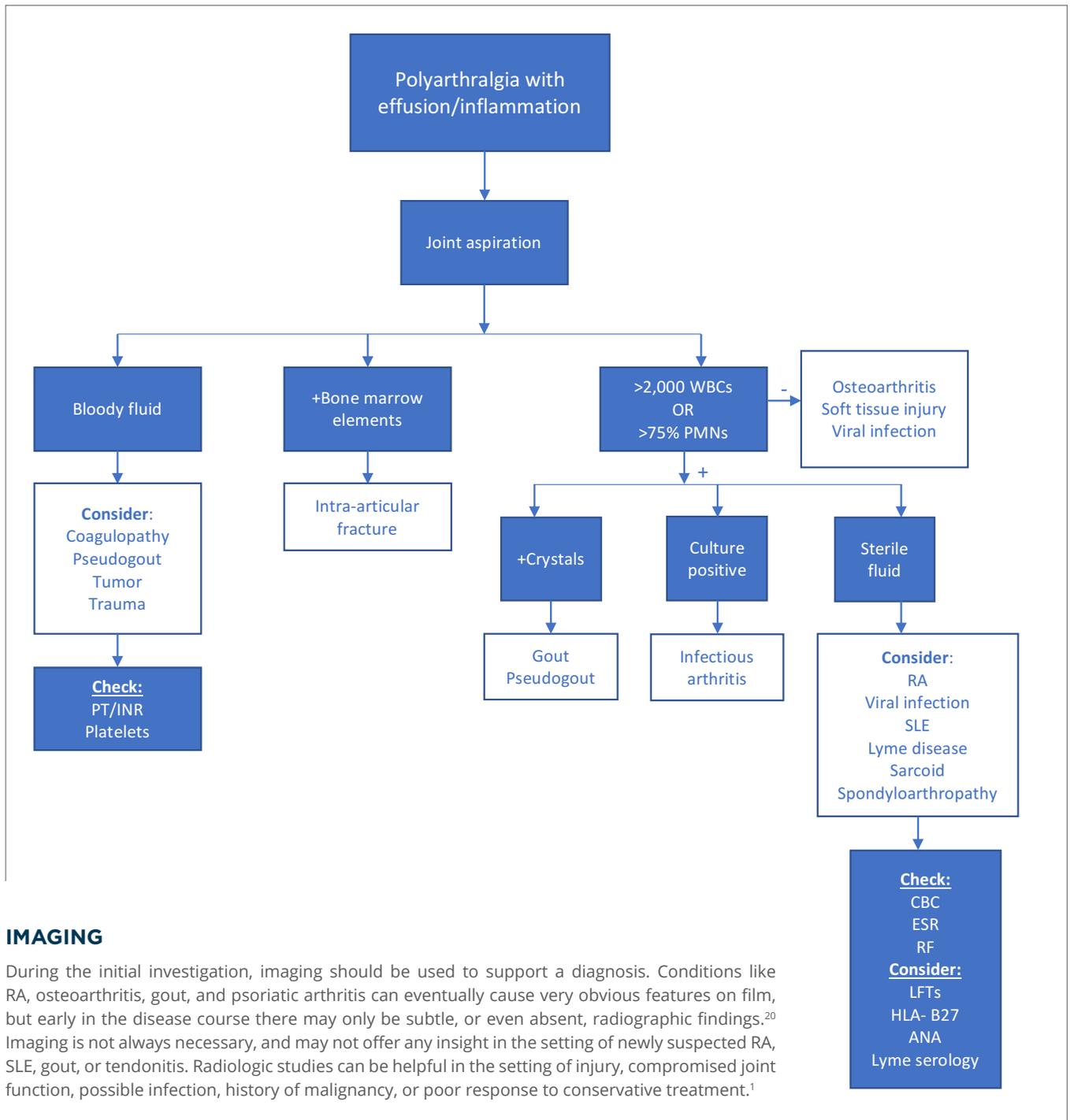
While uric acid in excess can predispose individuals for developing gout, hyperuricemia alone is not diagnostic for the condition.<sup>18</sup> Measuring serum uric acid during a suspected attack does not aid with diagnosis, as uric acid levels may be normal or even low during this time. Uric acid levels become useful for monitoring chronic gout.<sup>1</sup>

### Synovial Fluid

Analysis of synovial fluid becomes a very important diagnostic modality when a crystal-induced arthritis or infection is suspected. In order to confirm these diagnoses, the joint must be aspirated. It is important to send the fluid for Gram stain and culture, cell count, and microscopy to identify crystals.<sup>4</sup> Gout is diagnosed with the presence of monosodium urate crystals which are negatively birefringent on microscopy.<sup>4,18</sup> Synovial fluid containing at least 2,000 per mm<sup>3</sup> of white blood cells is considered inflammatory in nature. If the sample contains over 50,000 per mm<sup>3</sup>, infection is likely (*Table 3*).<sup>19</sup> Fluid culture will confirm the presence of bacteria and guide the proper antibiotic treatment. While cell counts and culture are pending, any patient with fever and joint effusion should be treated with concern for septic arthritis<sup>4</sup> (See *Table 3*, *Figure 2*).

FIGURE 2:

Interpretation of synovial fluid aspirate<sup>1</sup>



**IMAGING**

During the initial investigation, imaging should be used to support a diagnosis. Conditions like RA, osteoarthritis, gout, and psoriatic arthritis can eventually cause very obvious features on film, but early in the disease course there may only be subtle, or even absent, radiographic findings.<sup>20</sup> Imaging is not always necessary, and may not offer any insight in the setting of newly suspected RA, SLE, gout, or tendonitis. Radiologic studies can be helpful in the setting of injury, compromised joint function, possible infection, history of malignancy, or poor response to conservative treatment.<sup>1</sup>

On plain films, joint space narrowing is often used as a marker for potential articular cartilage damage in early osteoarthritis (OA), but studies show there is not a clear correlation, and this finding cannot accurately diagnose or rule out OA.<sup>21</sup> In early RA, conventional radiography may show nonspecific signs such as soft tissue swelling.<sup>1</sup> Identification of erosions early on has been shown to indicate likely progression of structural joint damage. As prompt treatment is required for good prognosis in RA, it is crucial to identify these early erosions. Ultrasound and MRI are found to better detect bone erosions than plain films, and can be very important in monitoring RA progression.<sup>22</sup> Conventional radiography is the first line in detecting structural damage from seronegative spondyloarthropathies such as ankylosing spondylitis, but MRI can be useful in detecting early inflammatory changes.<sup>23</sup>

## OSTEOPATHIC PRINCIPLES

Although there is no definitive evidence regarding the benefit of osteopathic manipulative treatment (OMT) in treating arthritic pain, some studies have shown that including OMT in the treatment for certain chronic pain syndromes is efficacious.<sup>24</sup> It is important to discuss the concept of facilitation while speaking of polyarthritis. Facilitation occurs when a segment of neurons remain in a state of partial or sub-threshold excitement. These groups of neurons enter a facilitated state when they receive input from a certain stimulus, which may be somatic in nature. Inflammation and tension at a joint can cause sensitization of a neuronal segment, resulting in facilitation of the segment. Over time, the facilitated segment can deliver hyperstimulated output to the region of the joint, resulting in tissue texture changes, restrictions, and tenderness, all of which will worsen the patient's condition. The sympathetic innervation for the upper extremities stems from T2-T8, while the lower extremities are innervated by T11-L2. These regions should be evaluated for tissue texture changes by the osteopathic physician. Physicians may choose to use myofascial release, articulation, and counterstrain techniques to normalize sympathetics and reverse facilitation to improve healing.<sup>25</sup>

## SUMMARY

In order to accurately diagnose a complaint of polyarthritis, the physician must employ an extensive history and physical to help narrow the broad differential. If there is a history of trauma or the patient presents with localized bone pain, appropriate imaging should be done to rule out fracture or a tumor. If synovitis is present for greater than 6 weeks, a systemic rheumatic disease must be ruled out through further testing (ESR, RF, ANA). If the synovitis is present for less than 6 weeks, the patient will require close follow up, as this may be a sign of early rheumatic disease or perhaps a viral arthritis. Patients found to have effusion often require joint aspiration for further evaluation. The contents of the aspiration can point to a likely diagnosis, and further testing may be required for confirmation. If there is no effusion or signs of inflammation at the joint site, the physician should evaluate whether there are trigger points or point tenderness. The presence of these focal findings can point to bursitis, tendinitis, or fibromyalgia. Lack of point tenderness may indicate osteoarthritis or a soft tissue injury.<sup>1</sup>

Primary care physicians are often the first clinicians to evaluate patients suffering from polyarthritis, and they are a crucial part in identifying patients who require prompt treatment to ensure the best possible outcomes.

## AUTHOR DISCLOSURES:

No relevant financial affiliations.

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