Approach to the patient with polyarthritis

How do polyarthritis, polyarthralgias, and diffuse aches and pains differ?
Polyarthritis is definite inflammation (swelling, tenderness, warmth) of more than four joints demonstrated by physical examination. A patient with two to four involved joints is said to have pauci- or oligoarticular arthritis.

Polyarthralgia is defined as pain in more than four joints without demonstrable inflammation by physical examination. The chronic noninflammatory arthritides commonly present with polyarthralgias.

Diffuse aches and pains are poorly localized symptoms originating in joints, bones, muscles, or other soft tissues. A joint examination does not reveal inflammation. Polymyalgia rheumatica, fibromyalgia, SLE, polymyositis, and hypothyroidism commonly present with these symptoms.

History

Time Course of Joint Symptoms
Polyarticular joint symptoms may have an acute or insidious onset.

Acute polyarthritis, especially when accompanied by fever, is always due to an inflammatory disease and requires immediate evaluation to rule out infection or crystalline arthritis.

Alternatively, there are both inflammatory and non-inflammatory causes of polyarthritis with an insidious onset.

Variations, however, may occur, and a disorder that typically has an insidious onset may have an acute onset in some patients.

Pattern of Joint Involvement
The additive pattern is most common but least specific. It refers to recruitment of new joints while previously involved joints remain involved and is commonly seen in RA and other systemic rheumatic diseases.

A migratory pattern refers to symptoms being present in certain joints for a few days and then remit, only to reappear in other joints. This pattern is most characteristic of rheumatic fever, the early phases of Neisseria infection and Lyme disease, and acute childhood leukemia.

An intermittent pattern is typified by repetitive attacks of acute polyarthritis with complete remission between attacks. Palindromic rheumatism, crystal-induced diseases, familial Mediterranean fever, and Whipple’s disease can intermittently affect joints for a few to several days at a time, followed by asymptomatic periods of varying length over a number of years.
RA, relapsing seronegative symmetrical synovitis with pitting edema (RS3PE syndrome), systemic lupus erythematosus (SLE), sarcoidosis, and Still’s disease can also appear episodically, particularly early in their disease course.

The seronegative spondyloarthropathies may have an intermittent course, but the articular symptoms in these diseases last for weeks (not days) at a time before resolving.

**Pain Characteristics**

Inflammatory joint pain involves the joints diffusely and is present at rest and with normal use. Nocturnal pain may interfere with sleep.

This joint pain is associated with prolonged stiffness for greater than 30 to 60 minutes, which is worse in the morning or after inactivity (gelling).

Fatigue is common, may be severe, and typically occurs by early afternoon after stiffness has improved.

Patients with non-inflammatory joint pain have pain with activity that is relieved by rest. Although they may have stiffness or gelling after inactivity, it typically lasts less than 15 minutes, and systemic fatigue is not common.

**Number and Distribution of Joint Involvement**

Polyarthritis refers to involvement of five or more joints. The joint distribution typically is symmetric, although distribution may go through an initial asymmetric phase.

The most common identifiable cause of a self-limited disorder causing acute symmetric polyarthritis involving the small joints of the hands and wrists is parvovirus-associated arthritis.

The most common cause of a chronic inflammatory polyarthritis that involves small and large joints bilaterally and symmetrically in the upper and lower extremities is RA.

The metacarpophalangeal (MCP) joints and proximal interphalangeal (PIP) joints of the fingers, metatarsophalangeal (MTP) joints of the feet, and wrists are commonly affected, while the distal interphalangeal (DIP) joints, lumbar spine, and sacroiliac joints are spared.

Inflammatory arthritis in an RA pattern but also involving the DIP joints of the fingers should always suggest psoriatic arthritis or multicentric reticulohistiocytosis.

Any patient with inflammatory arthritis involving both ankles predominantly should be evaluated for acute sarcoid arthropathy.

**A number of non-inflammatory disorders may cause a chronic polyarthritis.**
The most common of these is primary generalized osteoarthritis, which typically involves the DIPs, PIPs, and first carpometacarpal (CMC) joint of the fingers, hips, knees, and first MTP.

Hemochromatosis and calcium pyrophosphate disease (CPPD) should be considered in a patient with chronic non-inflammatory polyarthritis involving the MCPs, wrists, shoulders, and ankles, which are joints not typically involved with osteoarthritis.

**Associated Extra-Articular Symptoms and Medical Conditions**

The presence of past or current extra-articular manifestations may provide important clues to the etiology of polyarticular arthritis.

Fever suggests a subset of illness including infection (viral, bacterial), postinfectious (rheumatic fever, reactive arthritis), systemic rheumatic diseases (RA, SLE, Still’s disease, vasculitis, IBD), crystal-induced diseases (gout, pseudo-gout), and miscellaneous diseases (malignancy, sarcoidosis). Night sweats and weight loss may also be important.

Rashes such as psoriatic plaques, erythema migrans (Lyme disease), erythema nodosum (IBD, sarcoidosis), erythema marginatum (rheumatic fever), and butterfly malar rash (SLE), among others, can be particularly useful in the diagnosis.

Other potentially important diagnostic clues are a history of Raynaud’s disease, serositis, oral ulcers (IBD, Behçet’s disease), or involvement of the lungs, heart, kidney, or liver.

Other important associated symptoms include a history of diarrhea, abdominal pain, urethral discharge, low back pain, and uveitis, which may indicate a reactive arthritis or other spondyloarthropathy.

A review of a patient’s concomitant medical conditions, medications, travel, and social history is important.

Certain disorders, like renal insufficiency, obesity, and alcoholism, or use of medications such as diuretics and cyclosporine, among others, are associated with gouty arthritis, while hyperparathyroidism and hemochromatosis are associated with chondrocalcinosis and pseudogout.

The sexual history should be elicited to help exclude reactive arthritis, gonococcal arthritis, and human immunodeficiency virus (HIV) exposures.

A history of blood transfusions or intravenous drug use puts patients at risk for hepatitis B, hepatitis C, HIV, or septic arthritis.

The use of certain medications, such as procainamide, hydralazine, and minocycline, can cause drug-induced lupus.

Frequent exposure to children may predispose to par-vovirus infection and rheumatic fever.
Tobacco abuse may indicate lung cancer in a patient with hypertrophic osteoarthropathy.

**Physical Examination**

The physical examination should be used to verify the presence of historical features as well as additional findings the patient may have not reported.

Vital signs can help determine the severity of the illness with fever being most important.

Other findings on general examination that suggest a systemic disorder include:

- lymphadenopathy, parotid enlargement, oral and genital ulcers, eye disease (conjunctivitis, uveitis, scleritis, keratoconjunctivitis sicca, funduscopic abnormalities),
- heart murmurs (subacute bacterial endocarditis, rheumatic fever), bruits, pericardial or pleural friction rubs.
- fine inspiratory rales due to interstitial lung disease,
- hepatosplenomegaly,
- muscle weakness (polymyositis), and any neurologic abnormalities (vasculitis)
- Particular attention should be given to the skin and nails, looking for characteristic rashes or nodules (rheumatoid, tophi, or, rarely, xanthomas or amyloid masses).

In addition to symptomatic joints, all 66 joint areas should be examined.

Particular attention should be given to the spine examination to rule out an underlying axial arthritis.

Upon examination of the symptomatic joints, the presence or absence of synovitis should be documented.

The detection of synovitis limits the differential diagnosis to an inflammatory arthritis and is characterized by diffuse involvement of the joint with tenderness, soft tissue swelling, warmth over the joint, and possibly a joint effusion. Active and passive range of motion will be limited in all planes.

Significant erythema should suggest an infectious or crystalline arthropathy.

Crepitus may be heard or felt as the joint is put through a range of motion. Fine crepitus can arise from synovitis, while more medium crepitus can arise from grating of roughened cartilage surfaces or from bone rubbing against bone.

The examination of symptomatic joints in patients with a non-inflammatory arthritis typically shows diffuse involvement with tenderness, bony enlargement or spurs,
minimal if any warmth, and no erythema. An effusion, particularly in the knee, may be demonstrated. Range of motion is limited, both passively and actively, in all planes, and medium or coarse crepitus may be felt.

**Laboratory Studies**

A complete blood count, biochemical tests of renal and liver function, and a urinalysis may help to identify patients with a systemic illness.

Serum uric acid levels are usually elevated in gout but can be normal, particularly in patients with a polyarticular onset.

An elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are not specific but are elevated in over 90% of patients with an inflammatory cause for their polyarthritis.

Unfortunately, patients with non-inflammatory arthritides may have an elevated ESR/CRP because of another problem such as diabetes, dysproteinemia, or occult malignancy.

Specific antibody tests can identify exposure to potential pathogens such as Group A streptococcus (antistreptolysin O antibody), parvovirus B19, hepatitis B and C, Epstein–Barr virus, and Borrelia burgdorferi (Lyme disease) and should be ordered when these diseases are suspected clinically.

Rheumatoid factor should be ordered in patients suspected to have RA but can also be present in high titers in patients with other diseases which can cause a polyarthritis resembling RA, such as SLE, subacute bacterial endocarditis, and hepatitis C.

The ANA test has high sensitivity but low specificity for SLE. A negative ANA rules out SLE whereas a positive ANA with specific antibodies to double-stranded DNA or Smith (Sm) are virtually diagnostic of SLE in a patient with polyarthritis.

Synovial fluid should be obtained for total white blood cell count, crystal examination, and cultures when the diagnosis remains uncertain after history, physical examination, and standard laboratory tests.

Synovial fluid is only diagnostic in patients with infections, gout, and pseudogout. Otherwise, synovial fluid analysis can only classify the polyarthritis as inflammatory (>2000 WBC/mm3) or non-inflammatory based on the synovial fluid WBC count.

**Radiographic Studies**

In an appropriate clinical setting, plain radiographs may be supportive of a particular diagnosis.
The findings of chondrocalcinosis and osteoarthritic changes suggest, but do not prove, these diagnoses without corresponding synovial fluid analysis.

In acute polyarthritis, radiographs lack specificity and usually only show soft tissue swelling and intra-articular fluid.

In chronic inflammatory polyarthritis, marginal joint erosions are seen earliest in the small joints of the hands, wrists, and feet in patients with RA.

Chronic gout can also cause erosions with an overhanging edge that typically involve small peripheral joints such as the first MTP joint.

**Differential Diagnosis of acute polyarthritis**

Many acute viral infections cause joint symptoms, with polyarthralgias being considerably more common than true poly-arthritis. The prevalence of polyarthritis is high, however, in adults with acute erythrovirus (parvovirus B19) infection.

The pattern of viral polyarthritis often mimics that of rheumatoid arthritis. Adults with acute erythrovirus (parvovirus B19) infection, the cause of “slapped cheek fever” in children, usually have only a faint rash on the trunk or no rash at all.

IgM antibodies to erythrovirus (parvovirus B19) are generally present at the onset of joint symptoms and persist for approximately 2 months.

Acute hepatitis B causes an immune complex–mediated arthritis, often with urticaria or maculopapular rash, during the preicteric phase of infection; tests for hepatitis B surface antigen are positive.

PARVOVIRUS INFECTION

Adult and juvenile rheumatoid arthritis and psoriatic arthritis can present as acute polyarthritis but typically have a more insidious onset.

Both children and adults can develop Still’s disease, which is characterized by high spiking fevers, polyarthritis, pericarditis, an evanescent truncal rash, neutrophilic leukocytosis, and the absence of a rheumatoid factor and ANA. The fever characteristically spikes up to 104°F once or twice a day and returns to normal or below normal between fever spikes. The synovitis may be intermittent initially, but a persistent polyarthritis develops in most patients.

Systemic lupus erythematosus may present with acute polyarthritis that can be additive, migratory, or inter-mittent and may occur with fever. Characteristic rashes, other extra-articular manifestations, and a positive ANA support the diagnosis.

**Rheumatoid Arthritis**
Rheumatoid arthritis is the most common cause of a chronic inflammatory polyarthritis. Approximately 30% to 40% of patients presenting to an early polyarthritis clinic have RA.

Patients classically present with a symmetric polyarthritis that usually affects MCPs, PIPs, wrists, and MTPs.

Prolonged morning stiffness upon awakening and gelling after periods of inactivity are common.

Proliferative synovitis of symptomatic joints may lead to deformities and erosions on radiographs.

Extra-articular manifestations include subcutaneous nodules (25%), pleural effusions, episcleritis, and vasculitis, among others.

Rheumatoid factor is positive in 70% to 85% of patients, while anti-CCP is positive in only 50% to 60% of patients, but is more specific (95%).

**Psoriatic Arthritis**

Psoriatic arthritis can have several presentations.

The typical onset is as an oligoarticular arthritis that may evolve into a symmetric small and large joint polyarthritis resembling RA.

The involvement of the DIP joints, presence of psoriatic plaques, and the absence of rheumatoid factor support the diagnosis.

**Systemic Rheumatic Disease**

Systemic lupus erythematosus frequently presents as a symmetric polyarthritis that may be confused with RA if other extra-articular manifestations have not yet appeared.

The arthritis may be migratory or inter-mittent and extremely painful.

Synovial proliferation is not as evident as with RA but can lead to RA-like deformities. Notably, articular erosions are not present on radiographs, even in patients with a deforming arthritis.

Drug-induced lupus presents with a symmetric polyarthritis associated with systemic manifestations such as fever and serositis.

Other systemic rheumatic diseases can have an inflammatory polyarthritis, including mixed connective tissue disease and systemic sclerosis. Patients with these diseases will also have Raynaud’s disease and skin thickening.
Patients with polymyositis and dermatomyositis may have a polyarthritis accompanied by proximal muscle weakness and/or a characteristic rash.

**Other Systemic Illnesses**

Hepatitis C viral infection may be associated with a chronic polyarthritis resembling RA. These patients may have a high titer rheumatoid factor but negative anti-CCP antibodies and no erosions on radiographs. Cryoglobulinemia, hypocomplementemia, and vasculitis may be seen. Any patient with polyarthritis and elevated liver-associated enzymes should be evaluated for hepatitis C infection. Multicentric reticulohistiocytosis can also cause a destructive arthritis that mimics RA. Involvement of the DIP joints and the presence of periungual nodules should help define the diagnosis.

**Osteoarthritis**

Osteoarthritis is the most common cause of an asymmetric non-inflammatory polyarthritis as well as an asymmetric oligoarticular arthritis with or without axial involvement.

Primary generalized “nodal” osteoarthritis is an asymmetric non-inflammatory arthritis characterized by Bouchard’s nodes in the PIP joints and Heberden’s nodes in the DIP joints of the hands. Other joints characteristically involved are the first CMC, cervical and lumbar spine, hips, knees, and first MTP joints.

Pain is aggravated by weight bearing and motion. On examination, bony enlargement from osteophytes and crepitus from roughening of articular cartilage may be detected. Non-inflammatory synovial fluid may be detected as an effusion, particularly in the knees.