Introduction

About 15% of the patients in general practice present with complaints related to the musculoskeletal system. There is a large number of conditions which can cause these symptoms. The biggest fear in the mind of a patient is whether it is going to be a disabling 'arthritis'. Vast majority of the patients with musculoskeletal complaints suffer from self-limiting and benign ailments which technically would not even merit the name arthritis. However, superficial resemblance is close enough to create a good deal of confusion in the mind of the uninitiated physician. Indeed, it can be quite a challenge to arrive at the appropriate diagnosis. A good approach to differential diagnosis is, therefore, of paramount importance.

Importance of history and physical examination

A careful history provides 80% of the diagnostic information. Physical examination adds another 15% while imaging and laboratory together contribute only 5%. The following points are worthy of note in the history:

1. Duration of complaints (acute versus chronic).
2. Number of joints involved (mono, oligo or polyarthritis).
3. Distribution of joints involved (peripheral, axial, sparing some joints)
4. Pattern of involvement (recurrent, additive, migratory etc.)
5. History of joint swelling
6. Duration of early morning stiffness (prolonged in inflammatory arthritis)
7. Extra-articular complaints (e.g. fever, rash, alopecia, oral ulcers, photosensitivity etc.)
8. Associated medical illness (e.g. psoriasis, hypothyroidism, tuberculosis, IBD)
9. Significant past history (similar episode of arthritis, drug allergy, peptic ulcer)
10. Family history of rheumatic disease (e.g. gout, spondarthritis)

Physical examination should be able to define the abnormality in the locomotor system e.g. various extra-articular lesions and evidence of synovitis in the joint. When pain arises from the joint, the following observations are helpful:

1. Presence of swelling of joint (synovial fluid, bony)
2. Local warmth (as in inflammatory arthritis)
3. Tenderness along the joint line
4. Redness (e.g. septic arthritis, acute gout, etc.)
5. Range of motion (often reduced)
6. Any deformity

Differential Diagnosis

From the community perspective, vast majority of the patients with musculoskeletal complaints suffer from back pain (48%), other soft-tissue rheumatism (12%), osteoarthritis and other non-inflammatory arthritides (31%). Only a minority of patients suffer from the inflammatory joint disorders (9%). No wonder, most of such patients are managed by general practitioners, physical medicine and rehabilitation specialists and orthopaedicians. Patients with inflammatory joint disorders (systemic rheumatic disorders) tend to get
selectively referred to rheumatologists because of the difficult problems posed by these diseases. Thus, the spectrum of patients presenting to the Rheumatology Clinic of AIIMS comprises inflammatory rheumatic diseases (80%), soft-tissue rheumatism (10%) and osteoarthritis (10%). Sometimes bone pains arising from diffuse bone disorders (metabolic, neoplastic, haematological etc.) may mimic a rheumatic disease and it is important to remember this miscellaneous category.

There are five major steps involved in the differential diagnosis:

**Step I: Is it soft-tissue rheumatism?**

This issue must be addressed first of all because soft-tissue rheumatism (STR) is the commonest cause of musculoskeletal pain. A detailed discussion is outside the purview of this article but the various entities are listed in table I. In general, it may be remembered that in STR, pain is elicited by active but not passive movement of joint. The tenderness tends to be away from the joint-line. Periarticular swelling may be produced by tenosynovitis, tendonitis and bursitis. Local steroid injection produces dramatic relief in symptoms in many of these conditions.

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enthesopathy</td>
<td>Tennis elbow, golfer’s elbow, plantar fasciitis</td>
</tr>
<tr>
<td>Bursitis</td>
<td>Subacromial, olecranon, trochanteric, ischial, anserine, retrocalcaneal</td>
</tr>
<tr>
<td>Tenosynovitis</td>
<td>Volar flexor, DeQuervain’s, trigger finger</td>
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<tr>
<td>Tendonitis</td>
<td>Rotator-cuff, bicipital, Achilles’s</td>
</tr>
<tr>
<td>Entrapment neuropathy</td>
<td>Carpal tunnel, tarsal tunnel, meralgia paresthetica</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Dupuytren’s contracture, Tietze’s syndrome, adhesive capsulitis, repetitive strain syndrome</td>
</tr>
</tbody>
</table>

Many patients presenting with the above (localised syndromes) may have one of the following generalised disorders:

- Fibromyalgia syndrome (chronic pain-amplification syndrome)
- Chronic fatigue syndrome
- Benign joint hypermobility syndrome (BJHS)
- Psychogenic rheumatism

It is important to identify the underlying condition and institute appropriate therapeutic measures. Benign joint hypermobility syndrome is particularly common in Indians. However, it is a diagnosis of exclusion and associated inflammatory rheumatic disorder must not be overlooked.

**Step II: Is it inflammatory arthritis?**

Inflammatory arthritis is characterised by:

1. Some or all of the 4 cardinal signs of inflammation (swelling, warmth, pain, erythema)
2. Prolonged early morning stiffness (usually about 60 minutes or more)
3. Improvement of symptoms on gentle use of joints
4. Spontaneously fluctuating course
5. Usually symptoms are worse at night
6. Constitutional symptoms (fatigability, loss of appetite, loss of weight, low-grade fever or night sweats)
7. Presence of inflammatory markers: High ESR, CRP and platelets, Reversed A/G ratio, Low haemoglobin, WBC may be high, Mild elevation of alkaline phosphatase

*(Synovial fluid examination is not always essential for proving inflammatory nature of arthritis)*

**Step III: Is it a monoarthritis?**

After it has been ascertained that patient has an inflammatory arthritis, the question whether patient has a monoarthritis must be addressed first. Although it may sound strange, many times a patient presenting with an obvious monoarthritis, turns out to have multiple joints inflamed, on careful examination. A monoarthritis could be acute (< 6 weeks) or chronic (> 6 weeks).

(a) **Acute Monoarthritis**

This is to be treated as a rheumatological emergency. Urgent synovial fluid examination mandatory for:

1. Pathogens (Gram staining, bacterial culture)
2. Crystals (polarised light microscopy)
3. White cell count

**Differential diagnosis of acute monoarthritis includes:**

1. Septic arthritis
2. Crystal arthropathies
3. Haemorrhagic arthropathies
4. Miscellaneous: Palendromic rheumatism, others
   Monoarticular onset of chronic inflammatory arthritis
   (frequently seen in psoriatic arthritis, may occur in RA
   and seronegative inflammatory arthritides)

ptic Arthritis:
(a) Gonococcal: This occurs in normal healthy young
   persons, more often in females, migratory
   polyarthralgia may precede, rash and tenosynovitis
   is common; synovial fluid lactate is normal. Rapidly
   responds to therapy.
(b) Non-gonococcal: Occurs in immunocompromised
   host or compromised joint(s): e.g. background joint
   disease, joint prosthesis, debilitating diseases,
   extremes of age; common pathogens include:
   Staphylococcus (aureus-50%, albus 10%),
   streptococci (20%), gram negative infections (15%),
   anaerobes and others (5%); synovial fluid lactate
   elevated. Response to treatment is slow, with 10%
   mortality.

ystal arthropathies:
   Gout
   Pseudogout
   Miscellaneous

Diagnosis of crystal arthropathies is straight forward in
the appropriate clinical setting. One must take into account
the age and sex of the patient, any underlying disease, any
medications being taken, etc. Synovial fluid examination is
agnostic of crystal arthropathy. In gout, one finds needle-
shaped, negatively birefringent crystals while in
pseudogout, the crystals are rhomboid shaped and positively
birefringent. It is an important category of arthritis where
treatment is very rewarding.

aemorrhagic arthropathies
   These may occur in patients with clotting disorders such
   as haemophilia or those on anticoagulants. Usually, large
   joints are involved.

onic monoarthritis
   Monoarticular presentation of chronic inflammatory
   polyarthritis (RA, psoriatic arthritis)

Chronic bacterial infection (tuberculosis, brucellosis,
   rare infections etc.) Rare conditions (villonodular synovitis,
   tumours, etc.)

Synovial fluid examination and/or biopsy is mandatory
for establishing the diagnosis. (Synovial fluid PCR for
   M.tuberculosis gives inconsistent and unreliable results)

Step IV: Differential diagnosis of inflammatory oligo/
polyarthritis

(a) With prominent extra-articular features
   SLE
   Systemic sclerosis
   Dermato/polymyositis
   Sjogren's syndrome
   Systemic vasculitis
   Adult-onset Still's disease
   Reactive arthritis/Reiter's syndrome
   Psoriatic arthritis
   Rheumatic fever
   Infective endocarditis
   Erythema nodosum syndrome
   Weber Christian disease
   Loefgren's syndrome
   Poncet's arthritis
   Behcet's syndrome
   Inflammatory bowel disease
   Chronic tophaceous gout
   Hyperlipidaemia
   Multicentric reticulohistiocytosis

   The above conditions are characterised by distinct extra-
   articular features, which are often of diagnostic value.
   Diagnostic criteria exist for most of these and will not be
discussed here.

(b) With predominant articular involvement
   (i) Acute (<6 weeks)
      Reactive arthritis
      Viral arthritis
      Postviral arthritis
      Drug-induced arthritis
      Poncet's arthritis
      Sarcoidosis
   (ii) Chronic (>6 weeks)
      Rheumatoid arthritis
      Spondarthritides (AS, Reiter's, IBD-associated, uSpA, juvenile
      spondylitis, PsA)
      Psoriatic arthritis
      JIA

   Classical reactive arthritis consists of a sterile
   oligoarthritis involving large joints, 1-3 weeks following
an infection either in the gut (salmonella, shigella, yersinia, campylobacter) or in the urogenital tract (chlamydia, ureaplasma). The typical triad of urethritis, conjunctivitis and arthritis (Reiter’s syndrome) is rarely seen. Examples of reactive arthritis accompanying primary tuberculosis (Poncet’s disease), streptococcal pharyngitis (Rheumatic fever, poststreptococcal reactive arthritis), Hansen’s disease and other infections are considered ‘non-classical’.

Sarcoid arthritis presents typically with bilateral ankle involvement with marked periarticular oedema. It usually responds to simple measures such as NSAIDs and physiotherapy. Polycyclic and chronic presentations can occur, occasionally.

The diagnosis of rheumatoid arthritis and spondarthritis is established with the recognition of typical distribution of joint involvement. Typically, RA is a peripheral, symmetrical polyarthritis, involving hands in 95% of cases with selective sparing of DIP joints. Spinal involvement is confined to cervical region only. Rheumatoid factor is useful more for prognosis than for diagnosis of RA. In spondarthritis, inflammatory back/buttock pain, with or without asymmetrical oligo/polyarthritis predominantly in the lower extremity with enthesitis presents a distinct clinical picture. Undifferentiated spondarthritis is the commonest entity in this group. In selected cases of spondarthritis, HLA typing may help in differential diagnosis. For the diagnosis of ankylosing spondylitis, sacro-iliitis (B/L grade II or unilateral Grade III) is essential. Psoriatic arthritis must be remembered as a great mimic of RA although usually, the diagnosis is quite obvious. Occasionally, skin involvement may follow arthritis by several years.

Step V: Is it a non-inflammatory joint disease?

Table 2 gives the various causes of non-inflammatory joint disorders. Classically, OA has a typical distribution of joint involvement: Knee joints, DIP, PIP and first CMJ involvement in hand with sparing of MCP joints. Early morning stiffness typically lasts 30 minutes or less. Sometimes, joint fluid can be aspirated but it is typically ‘non-inflammatory’. Radiographs show new bone formation in the form of osteophytes, usually lack of periarticular osteopaenia and erosions. The inflammatory markers such as ESR, CRP are not elevated.

**Table 2 Causes of non-inflammatory joint disorders**

| Osteoarthritis |
| Endocrine disorders (most notably, hypothyroidism) |
| Amyloidosis |
| Avascular necrosis |
| Neuropathic arthritis |
| Rare metabolic disorders (ochronosis, haemochromatosis, Wilson’s disease etc.) presenting as premature OA |

The following flow-chart gives an approach to differential diagnosis of musculoskeletal complaints:

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Musculoskeletal pain
  /       \
Bone disorders  Soft-tissue rheumatism  Arthritis
    |        |                        |
  Inflammatory Non-inflammatory
    |        |
  Monoarthritis  Oligo/polyarthritis
    |        |
  Acute  Chronic
    |        |
  With prominent E/A features  Predominantly articular disease
    |        |
  Acute  Chronic
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References