Meet the Expert
"Diagnosing Infective Polyarthritis"

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Hall G
8.00 to 10.00 hrs.

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Present attachment:
Meet the Expert

"Diagnosing Infective Polyarthritis"

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A Patient with Musculoskeletal (MSK) Pains - Clinical Approach

Abstract

Joint complaints make an important component of MSK diseases. In this write-up the importance of a strong clinical approach for categorising joint diseases based upon the number of involved joints (monoarthritis or polyarthritis), duration of disease (< 6 weeks – acute; ≥6 weeks – chronic) and whether the problem is inflammatory or non-inflammatory in nature, has been highlighted. Classifying patients on these clinical grounds helps in streamlining their management (e.g. primarily a problem of physician-rheumatologist, a physiatrist – rehabilitation expert or a joint surgeon). It provides the most satisfactory management strategy for such patients.

Introduction

Approximately a quarter of patients attending any general outpatient clinic have complaints related to musculoskeletal (MSK) system [1]. It is ironical that despite such high prevalence and impact of MSK diseases, this is not reflected in the medical curriculum; in most medical schools the undergraduates do not get enough training and exposure to MSK diseases; these are generally neglected by every one [2-5]. The Faculty of Medicine, Kuwait University, however, has been fortunate. The founders of the medical faculty realised the importance of MSK disease. A separate teaching block has been reserved for MSK system from the outset of the medical course. Over the years MSK system teaching of medical students has become more and more refined in Kuwait. With the final report of the undergraduate medical curriculum for MSK diseases already published [6], it is expected that Kuwait University would also incorporate these suggestions in their teaching of MSK diseases.

When confronted with a patient with MSK symptoms most doctors feel uncomfortable because of their lack of clinical training in this speciality. Therefore, by default such patients reach orthopaedic surgeons for help. Unfortunately, a significant proportion of patients with MSK diseases have serious systemic / multisystem / multi-organ problems that could be life-threatening – the so-called ‘RED FLAG MSK DISEASES’. Orthopaedic surgeons have little to offer to such patients. On the other hand, a large proportion of patients with MSK diseases have mechanical / structural, or local / regional conditions, the so-called ‘GREEN FLAG MSK DISEASES’. These conditions require help of physical medicine and rehabilitation experts (physiatrists) and experts in orthotics and appliances along with orthopaedic surgeons who could step-in if physical modalities of treatment and orthotic appliances fail to provide relief. Under these circumstances there are 2 possible options to help the patients with MSK diseases:

The first option is that the primary-care physicians / general physicians acquire expertise to distinguish ‘red flag’ musculoskeletal diseases from the ‘green flag’ musculoskeletal diseases. Then, patients could be referred to a physician-rheumatologist for the management of ‘red flag’ MSK diseases while those with ‘green flag’ MSK diseases get referred to experts in physiatry / orthotics / orthopaedic surgeons.

The second option is to have the discipline of ‘Rheumatology and musculoskeletal diseases’ where a team consisting of a physician with expertise / training in MSK diseases
The rheumatologist, a physiatrist with expertise in physical medicine and rehabilitation, a specialist in orthotic devices, and orthopaedic surgeon with expertise in joint and soft-tissue surgery, work together as a team to provide the best possible management. In most of the advanced medical centres around the world second approach is being followed with great patient satisfaction.

This write-up sharply focuses on the main clinical features that distinguish ‘red flag’ musculoskeletal diseases from ‘green flag’ musculoskeletal diseases. It has been observed that competence in distinguishing inflammatory from non-inflammatory MSK diseases is crucial for the training of medical students in dealing with MSK diseases later in their career. In a recent report 78% of the Resident doctors failed to demonstrate this basic competency [7].

Demography and Epidemiology of MSK Diseases

MSK diseases are usually considered problems of aging population. Most often elderly persons suffer from wear-and-tear related mechanical/structural problems of the MSK system i.e. osteoarthritis. However, more serious varieties of MSK diseases, the so-called ‘red flag’ conditions, occur more often in persons in the younger age group. Thus, most of the crippling, disabling or life-threatening MSK diseases occur in persons below fifty years of age and much more often in women. Even the paediatric age group is not spared as some of the more serious inflammatory diseases of the MSK system occur in children. Some common MSK diseases occurring in different age groups are given in table 1. Classifying MSK diseases based on age of onset is a convenient clinical method for narrowing down diagnostic possibilities.

In recent years the topic of ‘clinical approach to joint disease’ has been addressed by several authors [8-11]. The approach described below is based on these articles and their application in day-to-day clinical practice.

Classification of MSK Diseases

For a clinician classifying MSK diseases based upon distinction between ‘inflammatory’ vs. ‘non-inflammatory’ is most practical and useful. Yet, studies have shown that this crucial point is not adequately emphasised during undergraduate teaching of MSK diseases [12, 13]. Clinically such distinction is important because it helps in categorising serious systemic illnesses with bad prognosis from mechanical/structural/local/regional MSK conditions that are not life-threatening (table 2).
A Patient with Musculoskeletal (MSK) Pains - Clinical Approach

Table 2: The main 2 categories of musculoskeletal (MSK) diseases

<table>
<thead>
<tr>
<th>NON-INFLAMMATORY MSK CONDITIONS (The ‘Green flag MSK diseases’):</th>
<th>INFLAMMATORY MSK CONDITIONS (The ‘Red flag MSK diseases’):</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Mechanical / structural problems.</td>
<td>• Serious systemic problems with:</td>
</tr>
<tr>
<td>• Local and regional problems.</td>
<td>• Definite objective swellings in the joints, other physical findings.</td>
</tr>
<tr>
<td>• Psychogenic and somatisation:</td>
<td>• Gross laboratory abnormalities e.g. ESR, platelets etc.</td>
</tr>
<tr>
<td>• Diffuse aches and pain months/years,</td>
<td></td>
</tr>
<tr>
<td>• No objective signs ever except multiple tender spots!</td>
<td></td>
</tr>
</tbody>
</table>

Clinical evaluation of patients with MSK Diseases

The basic aim of the clinical evaluation of patients with MSK is the same as in any clinical situation, namely:

2. Establishing an exact diagnosis within these categories.
3. Identify the complications of the disease.
4. Assess the structural damage and functional disabilities.
5. Recognise the co-morbid conditions for appropriate planning of the treatment.

Among patients with MSK diseases it may not always be possible to establish an exact diagnosis in early stages. Yet, from the management stand-point it would suffice to classify them into ‘inflammatory’ and ‘non-inflammatory’ categories and initiate the preliminary treatment till the final diagnosis is reached.

Patients with musculoskeletal problems could have any of the following presenting complaints:

- Joint pains.
- Arthritis / arthralgias; (“I have arthritis!”)
- Joint swelling (synovial, effusion, bony).
- Diffuse musculoskeletal pains. (“I have pains all over body”!)
- Stiffness that sets in on immobility of the joints.
- Back pain.

The anatomical basis of pain arising in MSK system could be:

- **Joint**
  - Synovium - synovitis
  - Joint capsule - capsulitis
- **Periarticular - soft tissue:**
  - Bursa - bursitis.
  - Tendon sheath - tenosynovitis.
  - Tendon - tendonitis
  - Insertion of tendon, ligaments – enthesitis.
- **Bone**

Clinically it is important to distinguish whether the pain is arising from the joint (i.e. arthritis) or from periarticular soft tissue (soft tissue rheumatism) or bone (bone diseases).
Pain arising from periarticular soft tissue can be easily differentiated from that arising from joint on clinical grounds. Thus, the pain of soft-tissue rheumatism has the following characteristics:

- Pain elicited with active but NOT on passive movements.
- Tenderness away from the line margin.
- Swelling usually away from the joint (but periarticular swelling may be caused by these conditions).
- Dramatic relief with local steroids injections in inflammatory conditions.

Pain caused by bone diseases may sometimes be difficult to distinguish from that from the joints. This is especially true of diffuse bone disorders (metabolic bone disease, multiple myeloma etc.) or the bone diseases occurring at multiple sites e.g. multi-site osteonecrosis, multi-site osteomyelitis. As a general rule the bone diseases cause symptoms that are much worse at night time. It is important to remember that this category must also be considered in the differential diagnosis of any MSK pains.

Once it is certain that the pain is arising from the joint(s) a focused clinical history would give away the diagnosis in most of the cases. Although a thorough history would include a large number of clinical points related to MSK system (e.g. site of pain, character of pain, radiation of pain, intensity of pain, duration of complaints, periodicity of pain, circumstances of onset, aggravating and relieving factors, associated features including the duration of early morning stiffness, extra articular manifestations etc.; any significant past history or history of rheumatic diseases in the family), in the clinical evaluation of a patient with musculoskeletal complaints the following points need special emphasis:

Point no. 1

Duration of joint pain – < 6 weeks; ≥ 6 weeks: acute or chronic.

Point no. 2

Number of involved joints – single joint (monoarthritis) or > 1 joint (polyarthritis)

It may sound simple but before labelling the disease as ‘monoarthritis’ one must carefully examine the patient for, it is not uncommon that the patient may be complaining of pain and / or swelling only in one joint while actually the physical examination would reveal the presence of inflammation in several additional joints.

Thus, after eliciting clinical history and confirming the number of the involved joints and the duration of the complaints, the problem of the patient could be classified into any of the following four categories:

- Acute monoarthritis.
- Chronic monoarthritis.
- Acute polyarthritis.
- Chronic polyarthritis.

Point no. 3:

The next and possibly the most important point in MSK diseases that needs to be ascertained is whether the MSK disease is:

- Inflammatory disease
  OR
- Non-inflammatory disease

It cannot be overemphasised that differentiation between inflammatory and non-
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Table 3: Clinical laboratory parameters indicative of inflammatory rheumatic disease

<table>
<thead>
<tr>
<th>CLINICAL</th>
<th>INVESTIGATIVE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjective</td>
<td>High erythrocyte sedimentation rate (Westergren, fasting).</td>
</tr>
<tr>
<td>Significant early morning stiffness (&gt;30 min at least).</td>
<td>Normocytic normochromic anaemia.</td>
</tr>
<tr>
<td>Symptoms improve on gentle use of joints.</td>
<td>Thrombocytosis (&gt; 400,000 / cmn).</td>
</tr>
<tr>
<td>Spontaneously up-and-down course (‘spontaneous flares’).</td>
<td>White blood cell count may be high.</td>
</tr>
<tr>
<td>Constitutional symptoms (e.g. fatigue, loss of appetite, loss of weight, low-grade fever / drenching night-sweats).</td>
<td>Reversed albumin / globulin ratio.</td>
</tr>
<tr>
<td>(presence of any one or more of the symptoms indicate inflammatory musculoskeletal problem)</td>
<td>Moderate elevation of alkaline phosphatase.</td>
</tr>
<tr>
<td>Objective</td>
<td>High C-reactive protein levels.</td>
</tr>
<tr>
<td>Presence of local signs of inflammation (difficult to elicit in chronic cases).</td>
<td></td>
</tr>
</tbody>
</table>

**inflammatory MSK diseases** makes all the difference between satisfactory or unsatisfactory management of the patients. Clinical history, physical examination and laboratory investigations that help in distinguishing the inflammatory from non-inflammatory MSK diseases are given in **Table 3**.

Clinical evaluation would thus help in categorising the patients into the following: true arthritis, **Local/regional MSK problem** (soft-tissue rheumatism, periarthritis), bone disease (osteonecrosis, osteoporosis, others).

Arthritis could be classified into any of the 8 following categories:

**Acute** (< 6 weeks)  **Chronic** (≥ 6 weeks)

<table>
<thead>
<tr>
<th>Inflammatory</th>
<th>Inflammatory</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Monoarthritis</td>
<td>3. Monoarthritis</td>
</tr>
<tr>
<td>2. Polyarthritis</td>
<td>4. Polyarthritis</td>
</tr>
<tr>
<td><strong>Non-inflammatory</strong></td>
<td><strong>Non-inflammatory</strong></td>
</tr>
<tr>
<td>5. Monoarthritis</td>
<td>7. Monoarthritis</td>
</tr>
<tr>
<td>6. Polyarthritis</td>
<td>8. Polyarthritis</td>
</tr>
</tbody>
</table>

**Inflammatory arthritis** are further categorised in:

- Arthritis with **predominant articular involvement**.
- Arthritis with **prominent extra-articular manifestations**.

Careful review of systems would help in this distinction. Particular emphasis should be given to the involvement of:

- Skin, mucosa.
- Eyes.
Inflammatory polyarthritis presenting \textit{predominantly with articular symptoms} is further classified into:

\begin{itemize}
  \item \textbf{Seropositive arthritis} - prototype \textit{rheumatoid arthritis} (SPRA).
  \item \textbf{Seronegative inflammatory polyarthritis} (SNIPA) – often called ‘mimics’ of rheumatoid arthritis.
\end{itemize}

Clinical distinction between these two categories may not always be possible, especially in the early stages of the disease before the pattern of joint involvement and extra articular features are fully evolved. Usually the \textit{number and pattern} of joint involvement associated with the \textit{extra-articular features} help in distinguishing the two categories. Thus, whether it is an \textit{oligoarthritis} (2, 3 or 4 joints only), involves mainly the \textit{peripheral or mainly the axial joints}, involves mainly the \textit{lower segment} or equally affects both the \textit{upper and lower segments} of the body, specifically \textit{involves a certain joints or spares them}, is it a \textit{recurrent, additive or migratory joint disease}, a \textit{family history} of a certain disease(s) (e.g. psoriasis in a family member), are some of the \textit{clinical points that help in distinguishing different varieties of inflammatory arthritides}.

These fine distinctions are \textit{not necessarily meant for general practitioners} or primary care doctors. These are better left for the rheumatologists to worry about.

\textit{Inflammatory polyarthritis} presenting \textit{with prominent extra-articular symptoms} include the following conditions:

\begin{itemize}
  \item \textit{Skin and/or mucosal involvement is prominent:}
    \begin{itemize}
      \item Psoriatic arthritis.
      \item Behcet’s disease.
      \item Systemic lupus erythematosus.
      \item Scleroderma (systemic sclerosis).
      \item Dermatomyositis.
      \item Reiter’s disease.
      \item Cutaneous vasculitic syndromes.
      \item Panniculitides: erythema nodosum syndrome, Weber-Christian disease.
      \item Lofgren’s syndrome (acute onset sarcoidosis).
      \item Rare conditions: Multicentric reticulohistiocytosis,
    \end{itemize}
  \item \textit{Gastrointestinal symptoms are prominent:}
    \begin{itemize}
      \item Inflammatory bowel disease.
      \item Enteropathic form of reactive arthritis.
    \end{itemize}
  \item \textit{Urogenital symptoms are prominent:}
    \begin{itemize}
      \item Urethritic form of reactive arthritis including Reiter’s disease.
    \end{itemize}
  \item \textit{Other systems:}
    \begin{itemize}
      \item Polymyositis (muscles).
    \end{itemize}
\end{itemize}
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- Sjögren’s syndrome (lacrimal, salivary and parotid gland involvement prominent, often with the involvement of other exocrine functions).
- Severe systemic necrotizing vasculitides (multisystem).
- Still’s disease and adult-onset Still’s disease (rash, throat, serositis, hepato-splenomegaly, lymphadenopathy).
- Rheumatic fever, infective endocarditis (heart).
- Poncet’s disease (tuberculous lymphadenitis or tuberculous focus at other sites).
- Chronic tophaceous gout (soft tissue deposits with inflammation; gouty kidney).

Characteristic extra-articular manifestations are very helpful in diagnosis. Most of the inflammatory polyarthritis are chronic with fluctuating course and spontaneous flares. However, several of them may present as acute inflammatory polyarthritis. Thus, rheumatoid arthritis is known to have an explosive onset presenting as acute inflammatory polyarthritis. Classical ‘reactive arthritis’ of urethritic and/or enteropathic variety (including Reiter’s disease) characteristically present as acute inflammatory arthritis with a tendency to evolve into its chronic form. Acute oligoarthritis is a common presentation of psoriatic arthritis. The same is true of polyarticular gout (almost always a man above 40 years of age). Systemic lupus erythematosus as well as severe systemic vasculitis often present with acute inflammatory polyarthritis. Behcet’s disease, Lofgren’s syndrome (acute sarcoidosis) erythema nodosum syndrome, infective endocarditis, acute rheumatic fever, Still’s disease and Adult-onset Still’s disease, Poncet’s disease, often present as acute inflammatory polyarthritis.

Is the patient presenting with a chronic non-inflammatory polyarthritis?

In this category osteoarthritis (OA), especially the primary generalised nodular variety, is the commonest condition. The involvement of small joints in the hands in a symmetrical fashion may be mistaken for rheumatoid arthritis. However, the elderly age group (always above the age of 50 years) with little constitutional symptoms and absence of features of a systemic inflammatory disease would be strong clinical pointers against inflammatory arthritis. Moreover, the pattern of involvement of hand joints is rather characteristic for OA. Thus, there is prominent involvement of the distal interphalangeal joints often with bony nodule formation (Heberden’s nodules). The disease may involve the proximal interphalangeal joints often with bony nodules (Bouchard’s nodules). This disease completely spares the metacarpophalangeal (MCP) joints, an important point of distinction from rheumatoid arthritis, which predominantly involves the MCP joints. Most other conditions in this category are uncommon or rare endocrine / metabolic conditions and include hypothyroidism-related joint symptoms, amyloidosis-joint disease, ochronosis, haemochromatosis, and Wilson’s disease (the last 3 metabolic conditions presenting as premature OA).

Is the patient presenting with an acute non-inflammatory polyarthritis?

This is an interesting question. Is there any such clinical condition? Possibly none. However, somatisation problems, fibromyalgia, psychogenic rheumatism and hysterical arthritis may present with ‘acute pains’ in the MSK without features of any systemic inflammatory disease.

Is the patient presenting with an inflammatory monoarthritis?

As mentioned above, an important question that must be addressed right at the outset is
weather the patient actually has monoarthritis and not a polyarthritis. It is not uncommon for the patients to complain of pain in one joint only; the most prominently affected one, without mentioning the minor pains that may have been present in some of the additional joints. Repeated questioning and a careful physical examination is the only sure way not to miss a case of polyarthritis that has been wrongly labelled as a monoarthritis.

Like polyarthritis, depending upon the duration of the symptoms, monoarthritis could also classified into 2 categories:

- **Acute inflammatory monoarthritis** (duration < 6 weeks).
- **Chronic inflammatory monoarthritis** (duration ≥ 6 weeks).

### Acute inflammatory monoarthritis

Acute inflammatory monoarthritis is a rheumatological emergency. Making a precise diagnosis urgently is a priority. Delay in instituting appropriate management may prove disastrous. (Note: Be sure that it is actually monoarthritis as careful clinical assessment may show that the patient actually has more than one joint involvement). Presence of the 5 classical signs of acute inflammation (red, hot, tender, swollen and non-functional) make it easy to put the label ‘acute inflammatory’ joint disease. Urgent synovial fluid examination in these patients is mandatory.

The aspirated synovial fluid must be immediately examined for:

- **Crystals** (under polarised light microscopy).
- **Pathogens** (gram staining and microbial culture).
- **White cell count** (≥ 2000/cmm is diagnostic of inflammatory joint disease).

It is to be noted that a high white cell count by itself does not distinguish between the three major causes of inflammatory diseases in the joints (see above, table 4). It is increased in all the three conditions that cause inflammation in the joint, irrespective of the aetiology. Thus, high white cell count in the synovial fluid does not always mean infection. The same is seen in immuno-inflammatory joint disease as well and in crystal deposition joint disease. Probably the commonest cause of acute inflammatory monoarthritis in daily practice is immuno-inflammatory (especially in younger persons and female sex i.e. monoarticular presentation of rheumatoid arthritis, SLE, psoriasis, reactive arthritis etc.). The second commonest cause is crystal deposition disease (mainly men above 40 years of age or those with chronic compromised renal function or on drugs {e.g. cyclosporine}). Septic arthritis is the least common cause of acute monoarthritis. Such individuals usually have a predisposing factor (immunocompromised state) or history of unprotected sexual contact (gonococcal arthritis). **However, considering that any delay in the treatment of septic arthritis would quickly lead to joint destruction, it may be prudent to**
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Table 5: Differential diagnosis of acute monoarthritis

<table>
<thead>
<tr>
<th>Acute monoarticular presentation of chronic inflammatory polyarthritis:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Frequent in psoriatic arthritis.</td>
</tr>
<tr>
<td>• May occur in rheumatoid arthritis and other seronegative inflammatory polyarthritides.</td>
</tr>
<tr>
<td>• Not uncommon in SLE.</td>
</tr>
<tr>
<td>But, it is a ‘diagnosis of exclusion’.</td>
</tr>
</tbody>
</table>

Crystal arthropathies

• Gout.  
• Pseudo-gout.  
• Uncommon ones.  

Clinical setting very important: Age and sex, any underlying disease, drugs being taken (diuretics, cyclosporine). Synovial fluid examination decisive for confirming the diagnosis.

Septic arthritis:

• *Gonococcal* in normal healthy young persons.
• *Non-gonococcal*: Immunocompromised host or compromised joint(s):
  • e.g. some background joint disease, joint prosthesis, underlying debilitating diseases, immuno-compromised conditions of any type including extremes of age;  
  • Mostly non-gonococcal (Gram negative infections, anaerobes, and other rare ones – fungal, Borrelia, parasitic etc.)

*initiate antibiotic treatment empirically before laboratory reports give a definitive diagnosis.*

Differential diagnosis of acute inflammatory monoarthritis is given in table 5.

Chronic inflammatory monoarthritis

This is a small yet important category of arthritis. Tuberculosis, brucellosis, fungal infection and rare parasitic joint infections (guinea worm disease) are some of the causes. The clinical dictum is that in any case of chronic inflammatory polyarthritis *synovial fluid microbiology and/or biopsy MUST* be performed to get the actual diagnosis. The treatment can then be planned accordingly. No other method of diagnosis is valid for this class of arthritis. (Synovial fluid PCR for *M. tuberculosis* gives inconsistent and unreliable results) This category also includes many cases with *monoarticular presentation of immuno-inflammatory arthritides* (e.g. rheumatoid arthritis, psoriatic arthritis, several other seronegative arthropathies, etc.). However, this category remains a *diagnosis of exclusion*, if the synovial fluid microbiological studies and the biopsy fail to show any definitive infective pathology then, the diagnosis of ‘idiopathic inflammatory monoarthritis’ would be appropriate. The treatment would be intra-articular steroids and synovectomy.

Is the patient presenting with a non-inflammatory monoarthritis?

Acute non-inflammatory monoarthritis

Internal derangements, trauma, bleeding in the joint due to any haemorrhagic diathesis (diseases, drugs), and palindromic rheumatism are some of the common causes of non-inflammatory monoarthritis. Careful history and joint aspiration for synovial fluid analysis would help in establishing the diagnosis. An important clinical point is that in haemorrhagic diathesis the large joints mainly the knee, are affected.

Chronic non-inflammatory monoarthritis

This is one of the least common categories of arthritis. *Neuropathic joint disease (Charcot’s joint)* in tertiary syphilis was common in yesteryears. However, in present times *diabetes mellitus with severe peripheral neuropathy is the commonest cause of Charcot’s joint* the most common site being the ankle joint. The other relatively uncommon condition causing chronic non-inflammatory
Villonodular synovitis. It is a rare non-inflammatory proliferative condition of synovium with deposition of pigment in the tissue. Diagnosis is established by biopsy of the synovium and the treatment is surgical. Rare synovial tumours may also present as a chronic non-inflammatory monoarthritis.

**Avascular necrosis of the bone – osteonecrosis**

It is a bone disease that may clinically resemble non-inflammatory arthritis. The multi-site osteonecrosis could be confused with a non-inflammatory polyarthritis while that localised to a single site may be a differential diagnosis of non-inflammatory monoarthritis. The list of causes for osteonecrosis is long. However, a history of prolonged steroid intake is probably the most important among them and an important clue its diagnosis. Obviously Cushing’s syndrome is one of its causes. It is of interest to note that osteonecrosis is also often seen in rheumatoid arthritis, systemic lupus erythematosus, systemic vasculitis, scleroderma and other collagen-vascular diseases even without steroid therapy. The other causes include trauma (including radiation, thermal and electrical), haemoglobinopathies, coagulopathies, bleeding disorders, alcoholism, pancreatitis, organ transplant, chronic dialysis, hypertriglyceridaemia, pregnancy (mainly 3rd trimester), sepsis and infections (HIV), rare conditions (decompression syndrome, Gaucher’s disease), and idiopathic variety. The distinction of osteonecrosis from actual arthritis may be difficult and may require MRI study to confirm the diagnosis.

**Basic Management Strategy for MSK Diseases**

It is beyond the scope of this presentation to discuss the details of treatment for different forms of musculoskeletal diseases discussed above. Only an outline of the management strategies is given below.

**Treatment of local, regional or non-inflammatory (mechanical/structural) musculoskeletal conditions; the so-called ‘Green flag’ musculoskeletal diseases:**

This group of conditions mainly requires advice related to the physical conditioning of the body (appropriate diet, weight reduction, general toning of the muscles by aerobic exercises), other physical measures including physiotherapy, occupational therapy, heat, cold and electrical treatments, ‘pool therapy’ and advice related to change in lifestyle for the protection of joint and musculoskeletal tissue damage in day-to-day use. Other physical devices including orthotic devices may also be necessary in some of these conditions. Medical treatment using drugs is mostly of little or no use in this group of diseases. Occasionally, in certain special situations local injection of corticosteroids may be very useful. Patient education and reassurance that these diseases are by and large non-crippling and not life-threatening, goes a long way in making the patients feel better.

**Treatment of inflammatory conditions; the so-called ‘Red flag’ musculoskeletal diseases:**

Unlike local/regional or non-inflammatory rheumatic diseases, inflammatory rheumatic diseases require immediate, often prolonged and complicated regiments of drug therapy. Recent studies have demonstrated that not only acute inflammatory MSK diseases but also, more importantly, chronic inflammatory polyarthritides should be considered a medical emergency [14,15]. This is because permanent joint damage sets in rapidly within a few weeks of the onset of inflammation in the joint and becomes irreversible within the first 2 years [16]. This has led to strong argument in favour of early aggressive treatment of RA with remission inducing drugs [14, 15, 17–20]. Delay in initiating remission inducing drugs may lead to poor outcome and permanent joint damage [17, 21]. Because of these evidences early aggressive treatment for RA has now become standard practice [18-20, 22-24. Thus, the present-day drug treatment protocol for treating
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inflammatory polyarthritis (prototype rheumatoid arthritis), recommends that if a 12-week course of nonsteroidal anti-inflammatory drugs fails to achieve complete remission, the patient MUST be referred to a rheumatologist for a detailed evaluation and planning for initiating remission-inducing drugs [22,25]. These include the so-called disease modifying drugs (DMARDs) and the newer biological response modifiers (BRMs) e.g. anti-tumour necrosis factor (anti-TNF) agents and anti-interleukin-1 [22,26]. The main DMARDs include methotrexate (the ‘anchor drug’), sulfasalazine, leflunomide and hydroxychloroquine [26,27]. These 2 classes of drugs are often combined to increase their efficacy [19,20,24,25,28]. Till recently, the combinations of DMARDs were mostly chosen on empirical basis. However, recent advances in the molecular basis of the efficacy of these drugs is promising a rational approach to combining DMARDs in the near future [29]. The anti-TNF agents include infliximab, etanercept and adalimumab. A new and very promising new BRM rituximab has recently been reported for inducing prolonged remission in RA [30]. The use of these drugs requires expertise and experience that may not usually be available at the primary care level. Therefore, it is strongly recommended that before the decision to start these medicines (or systemic corticosteroids) is taken the patient must have a rheumatology consultation, preferably within 3 months of the onset of the disease [O’Dell 2004].

Acknowledgement

The author wishes to thank Dr. Ashok Kumar, Professor of Medicine, Chief of Clinical Immunology & Rheumatology Services, Department of Medicine, All-India Institute of Medical Sciences, New Delhi for helpful discussions.

Summary

Musculoskeletal symptoms - diagnostic categories:

- **Arthritis**
  - Acute (≤ 6 weeks)
    - **Inflammatory**
      - Monoarthritis (Acute inflammatory monoarthritis)
      - Polyarthritis (Acute inflammatory polyarthritis)
    - **Non-inflammatory**
      - Monoarthritis (Acute non-inflammatory monoarthritis)
      - Polyarthritis (Acute non-inflammatory polyarthritis)
  - Chronic (≥ 6 weeks)
    - **Inflammatory**
      - Monoarthritis (Chronic inflammatory monoarthritis)
      - Polyarthritis (Chronic inflammatory polyarthritis)
    - **Non-inflammatory**
      - Monoarthritis (Chronic non-inflammatory monoarthritis)
      - Polyarthritis (Chronic non-inflammatory polyarthritis)

- **Soft tissue rheumatism**
  - Local
    - Bursitis
    - Tenosynovitis
- Tendonitis
- Enthesitis
- Regional
  - Foot pain, shoulder pain etc.
- Diffuse
  - Fibromyalgia
  - Psychogenic rheumatism
  - Somatisation of symptoms
- Bone disease
  - Local / multisite
    - Osteomyelitis, osteonecrosis, tumours etc.
  - Diffuse
    - Osteoporosis

Major diseases
- **Non-inflammatory** MSK diseases of including mechanical/structural i.e. ‘Green flag’
MSK diseases:
  - Non-inflammatory arthritides (mainly osteoarthritis; other non-inflammatory conditions
    including trauma-related, developmental problems, etc.).
  - Most soft-tissue rheumatisms
- **Inflammatory** MSK diseases i.e. ‘Red flag’ MSK diseases:
  - **Predominantly articular diseases** – prototype rheumatoid arthritis.
  - Those with predominant extra-articular features – psoriatic, seronegative inflammatory
    arthritis group, connective tissue diseases and vasculitides.

Approach to management
- **Non-inflammatory** (‘Green-flag’) MSK diseases:
  - Patient education
  - Physical medicine and rehabilitative measures
  - Corrective surgical interventions may be required
  - Minimum requirement for drug treatment, little role of rheumatologists.
- **Non-inflammatory** (‘Red-flag’) MSK diseases:
  - *Detailed rheumatological evaluation by a rheumatologist for exact diagnosis and planning
    drug treatment.*
  - Patient education
  - Physical medicine and rehabilitative measures
  - Corrective surgical interventions if and when required

References
2. Dequeker J, Rasker H. High prevalence and impact of rheumatic diseases is not reflected in the medical curriculum:
5. Reported by ‘Rheumawire’ Report (‘Rheumatalk’) April 10, 2002 ‘Residents inadequately trained in musculoskeletal medicine’ posted on the official website of ‘Joint and Bone’: jointandbone.org
Approach to the Patient with Polyarthritis

**Introduction**

In the evaluation of musculoskeletal diseases clinical history provides 80% of the information towards making a diagnosis. Additional 15% information is gathered from physical examination while laboratory investigations add only 5% information towards diagnosis [1]. Applying the same principle for the evaluation of a patient presenting with polyarthritis, a thorough clinical history remains the most important diagnostic tool. There are excellent write-ups describing clinical approach to polyarthritis. Reader is provided with a list of useful references for further reading [2-9]. Diagnosing polyarthritis is the most common intellectual exercise facing the rheumatologist but also the most rewarding. A skilled and experienced clinician using the ‘tools’ of history and physical examination can formulate a correct diagnosis and treatment plan. Although radiographs and certain laboratory tests are helpful, they should be used primarily as adjunct [8].

**Is It Polyarthritis?**

Within the category of polyarthritis i.e. involvement of more than one joint, many clinicians would further classify patients with only 2, 3 or 4 joint involvement as *oligo- or pauci-arthritis*. It often helps in making a diagnosis as it narrows down the diagnostic possibilities to only a few conditions (see below). *Thus polyarthritis is involvement of more than 4 joints.* It is important to point out, however, that quite often the entire attention of the patient is focused towards a single joint simply because that is the most symptomatic joint. A casual clinician may be misled to believe that the patient has monoarthritis. However, further probing of the history would easily reveal a polyarticular involvement where a single joint is more symptomatic than the others. There are conditions involving musculoskeletal systems that mimic polyarthritis. These must be carefully excluded before the condition is labelled as polyarthritis. *Table 1* gives the differential diagnosis of multiple sites of musculoskeletal pains that can mimic polyarthritis.

**Is Polyarthritis Acute or Chronic?**

By definition involvement of more than 4 joints of less than 6-week duration is classified as *acute polyarthritis*. Patients presenting with acute polyarthritis pose a major diagnostic challenge as this category includes almost every disease of importance in rheumatology some of whom could be potentially life-threatening and associated with high morbidity. Yet, in others it could simply be a benign self-limiting condition e.g. a postviral arthritis that resolves completely within 6 weeks. In the majority of acute polyarthritis cases definitive diagnosis is usually

*Table 1: Differential diagnosis of musculoskeletal pains that may mimic polyarthritis.*

- Multifocal osteonecrosis, periostitis, other primary bone diseases
- Muscle disorders
- Polymyalgia rheumatica
- Neuropathies
- Tendonitis, fibrostitis, multifocal bursitis
- Functional, fibromyalgia and malingering
Approach to the Patient with Polyarthritis

not possible at the outset. The reason is that by-and-large clinical rheumatology is a science of recognising pattern of joint involvement and its evolution and that still remains central to making a rheumatological diagnosis. Therefore, in acute polyarthritis the symptoms may not have yet evolved into a recognisable pattern for a definitive diagnosis. In some of them, a more detailed history including past history, family history, review of systems, physical examination and diagnostic evaluation may give a clue to the diagnosis. For example, acute dactylitis of a short duration in a young person by itself may not be diagnosable. However, history of psoriasis in a blood relative may provide a clue that in fact the person has acute presentation of psoriatic arthritis (PsA). But in others no such clue may be forthcoming. Therefore, most experienced rheumatologists realise that despite their best efforts only further evolution of pattern of symptoms over time may give a clue to diagnosis. It may be difficult for a young in-training rheumatologist to accept this ‘defeatist’ attitude but in clinical rheumatology it is no shame to wait-and-watch till either the symptoms resolve by themselves (benign self-limiting conditions) or evolve over time to become recognisable for making a definitive diagnosis. It may, however, be noted that future may be much brighter. Rapid advances in diagnostic techniques based on advanced technologies may be able to provide a diagnostic clue not only in the early stages of polyarthritis but even in preclinical stages. The best example is the presence of antibody against cyclic citrullinated peptides (anti-CCP antibody) [10]. Presence of high titres of these antibodies in a patient with acute polyarthritis is now considered a strong clue that it would evolve into rheumatoid arthritis (RA). Most rheumatologists would not wait for 6 weeks before embarking upon specific treatment for RA in such a patient. Thus, it is obvious that clinical rheumatology is an exciting and rapidly evolving field. The prevailing diagnostic paradigm may not hold true for too long. However, for the time being rheumatologists must follow the time-honoured methods of making a diagnosis.

Is the Polyarthritis Inflammatory in Nature?

Possibly the most crucial point related to making a diagnosis in polyarthritis (or for that matter in all forms of arthritis) is to evaluate whether it is inflammatory or non-inflammatory in nature [6]. This clinical point is pivotal as it determines the management and prognosis of the patient. A beginner or a non-rheumatologist clinician may not realise the importance of this distinction or mistakenly believe that presence or absence of time-honoured easily recognisable features of acute inflammation (namely red, hot, tender, swollen and non-functional) would be easily recognisable in joints for classifying polyarthritis as inflammatory or non-inflammatory. Unfortunately, the joints may be tender, swollen and non-functional even in non-inflammatory conditions e.g. osteoarthritis (OA) or traumatic arthritis. On the other hand, redness and local heat may not always be present or difficult to perceive even in inflammatory joint disease. For this reason, rheumatologists have devised an entirely different set of clinical features that distinguishes inflammatory from non-inflammatory joint diseases with high degree of sensitivity and specificity. Table 2 lists the clinical features

<table>
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<tr>
<th>Table 2: Clinical features to distinguish inflammatory from noninflammatory joint disease</th>
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<tr>
<td>1. Early morning stiffness that takes at least 30 minutes for maximum improvement, more often it takes about 1 hour for maximum improvement.</td>
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<tr>
<td>2. Activity (gentle movement) improves the symptoms but inactivity does not (inactivity may actually increase the stiffness).</td>
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<tr>
<td>3. Spontaneous ‘flares’ with fluctuation in the severity of symptoms over time without any obvious extraneous cause.</td>
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<tr>
<td>4. Constitutional symptoms: fatigue and tiredness, feverish feeling or actual fever, night sweats, loss of appetite and weight.</td>
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Note: Presence of one, more or all of these manifestations would strongly suggest the inflammatory nature of the joint problem with increasing probability.
that indicate the inflammatory nature of the joint disease. It is strongly recommended that clinicians get used to properly quizzing the patients about these symptoms by putting open-ended questions. For example a leading question ‘Are you stiff in the morning’? would be a wrong way of putting the question as against an open-ended question ‘How do you feel when you get up in the morning’?

If the clinical history suggests inflammatory polyarthritis, physical examination of the joints may reveal elevated temperature locally. Erythema or redness on the inflamed joints is usually not perceptible especially in those with dark skin. However, in those with intense inflammatory arthritis as seen in periankle-ankle involvement of acute sarcoidosis (Lofgren syndrome) and acute gouty arthritis involving joints in the feet, the overlying skin would show indurated inflammatory oedema with peeling off of the outer layer of skin as the inflammation subsides. However, in most of the common forms of inflammatory polyarthritides (RA, PsA) features of local inflammation may only be minimal or imperceptible.

**What is the Pattern of Joint Involvement?**

The next point to note in polyarthritis is the *pattern of evolution* of joint involvement. Basically there are 3 patterns namely *additive*, *intermittent*, and *migratory*. In additive pattern increasing number joints are progressively recruited with many joints getting affected over time. In *intermittent pattern* the joint involvement appears and then disappears till the next such episode with completely asymptomatic period in between these episodes. In its inflammatory form it is typically seen in palendromic rheumatism, acute gouty arthritis, relapsing polychondritis and relapsing seronegative symmetrical synovitis with pitting oedema (RS3PE). The last mentioned condition is associated with marked joint stiffness and symmetrical synovitis in the joints of the hands and feet. A condition called intermittent hydrarthrosis is an idiopathic noninflammatory intermittent arthritis. In *migratory pattern* the joints become symptomatic then subside while different joints get involved. The tempo of migration may differ for example it could be only hours between one to the next joint involvement in rheumatic fever. On the other hand the tempo of ‘migration’ may be much slower (days) in gonococcal arthritis. These patterns are not mutually exclusive but the dominant pattern may indicate a specific diagnosis.

The *topography or distribution of joint involvement* (which joints are affected in what distribution) usually helps in narrowing down the diagnostic possibilities. For describing the topography of joint involvement the following anatomical regions are taken in account: peripheral joints (in the extremities), axial joints (traditionally sacroiliac joints are considered part of axial joints), root joints (that overlap between peripheral and axial joints namely shoulder and hip joints), and upper segment and lower segment of the body (above and below waist). In peripheral joints symmetry or asymmetry is important to note. Thus inflammatory synovitis of small as well as large joints in the extremities in a symmetrical distribution on both sides of the body, equally distributed in upper and lower segment with predominant involvement of joints of the hands, wrists and feet, with sparing of the distal interphalangeal (DIP) joints, is rather typical of RA. Then, there are certain joints that, if involved in isolation or predominantly, may be a clue to diagnosis. Thus, involvement of DIP joints without synovitis or inflammation is typically seen in primary nodular OA but with synovitis, it is often seen in some subsets of PsA, enteropathic arthritis and sarcoidosis. Non-inflammatory involvement of the first carpometacarpal joint (floor of the ‘snuff-box’) is typically seen in primary OA. Similarly, noninflammatory first metatarso-phalangeal joint involvement is most commonly seen in OA. In acute gouty attack the same joint is often the first one to be affected with severe acute inflammatory response (podagra). Periankle-ankle inflammatory arthritis, (as mentioned earlier) usually associated with erythema nodosum is seen in acute
sarcoid arthritis (Lofgren syndrome). Acute dactylitis has already been mentioned to be strongly suspicious of psoriatic arthritis. Enthesitis (inflammation at the sites of insertion of ligaments, tendons to the bone such as Achilles tendonitis, planter fasciitis and others) associated with inflammatory axial joint involvement, sacroiliitis (classically presents with alternating buttock pain) and lower extremity asymmetrical inflammatory arthritis, often associated with root joint involvement is rather typical of spondyloarthritis (SpA) group. Prominent involvement of metacarpophalangeal joints without synovitis is typically seen in haemochromatosis. It needs to be emphasised, however, that pattern recognition as mentioned above is only a rough guide to diagnosis since there is considerable overlap in the pattern of joint involvement among different types of polyarthritis. Table 3 lists some of the common causes of polyarthritis classified as inflammatory vs. non-inflammatory further categorised on the basis of the topographic pattern of joint involvement. Figures 1 to 5 depict some of the typical topographic patterns of joint involvement in different forms of inflammatory and noninflammatory arthritides.

### Oligoarthritis
Involvement of 2 to 4 joints is called oligo-/pauci arthritis. Its separation from polyarthritis serves the purpose of narrowing down the diagnostic possibilities. Typically, inflammatory peripheral arthritis seen in the various forms of SpA is oligoarticular in nature with involvement of joints of the lower segment of the body with prominent asymmetry and associated enthesopathy. Table 3 gives a short list of conditions that commonly present with oligoarthritis. It is to be noted that almost all forms of inflammatory arthritides may evolve through oligoarticular stage but ‘true’ oligoarthritis would remain oligoarticular over time.

### Past, Personal and Family History; Review of Systems and Extra-Articular Involvement
Past history may have the clue for diagnosing polyarthritis. A transient episode of heel pain (Achilles tendon enthesitis, planter fasciitis) at juvenile age or an episode of uveitis in the past may be the clue to the present problem of inflammatory low back pain due to ankylosing spondylitis (AS). History in the recent past, of a febrile episode with or without exanthema, sexual contact or frank venereal disease, episode of diarrhoea, or acute conjunctivitis, may give a clue to the diagnosis of reactive arthritis, gonococcal arthritis or AS related peripheral arthritis. Quite often, past history may also unmask a diagnostic mistake made in the distant past e.g. history of ‘fever-of-unknown-cause’ in the past that was mistakenly either treated as typhoid or tuberculosis may actually have been an early manifestation of systemic lupus erythematosus that became overt in due course of time. Three most common diagnostic mistakes seen in day-to-day rheumatology practice involve tuberculosis, gout and rheumatic fever. It is quite common that a child or juvenile was given treatment for tuberculosis or rheumatic fever (long-acting penicillin) for months in the past for a mono- or oligoarthritis that evolved into rather typical SpA over time. The other common mistake is to diagnose and treat the patient as ‘gout’ (only based upon trivial increase in serum uric acid) over years while patient has been evolving into any of the common polyarthritides. Family history is equally important in making a diagnosis if polyarthritis. Similar disease (e.g. RA), or closely related autoimmune disease (thyroid, connective tissue disease, inflammatory bowel (IBD) disease, other autoimmune conditions) in the family members could be very useful in reaching a diagnosis. A so-called ‘seronegative inflammatory polyarthritis’ may actually be PsA (even in the absence of plaque psoriasis in the patient) if a blood relative is known to have plaque psoriasis. The significance of family history is more obvious in frank hereditary conditions e.g. AS and gout where invariably a positive history is elicited.
Inflammatory polyarthritis has bidirectional association with other organ systems of the body. On the one hand, it may affect different body parts and organs secondarily. On the other hand, by itself it may be part of a multisystem disease. Therefore, a detailed review of systems along with a careful general and systemic physical examination is mandatory.
for making an accurate diagnosis. History of skin, mucosal and subcutaneous lesions is highly relevant for making a diagnosis in a large number of inflammatory polyarthritis so much so that a rheumatologist has to be a good dermatologist. Thus, diagnosis of an otherwise undiagnosed ‘seronegative inflammatory polyarthritis’ becomes ‘PsA’ on discovering a psoriatic patch anywhere in the body, how-so-ever small it may be. Even a family history of psoriasis may help similarly. RA may have lesions of pyoderma gangrenosum (a form of neutrophilic dermatosis, also seen in IBD that itself may also be associated inflammatory polyarthritis, see below), subcutaneous nodules, and vasculitic lesions. Facial ‘butterfly’ rash of systemic lupus erythematosus (SLE) along with mucosal ulcers, alopecia and vasculitic skin lesions is diagnostic of the disease. Oral ulcers are seen in several other polyarthritis
including Behcet's disease (very painful commonly associated with genital ulcers), IBD related arthritis, and SpA. Gottron’s papules, heliotrope-facial rash, ‘mechanic’s hands’, ‘shawl sign’ along with periungual vasculitic infarcts are typical of dermatomyositis. Raynaud’s phenomenon associated with scleroderma skin changes including telangiectasia are typical of the disease and must be distinguished from seleredema of Bushke (no Raynaud’s phenomenon). Sarcoid skin lesions including lupus pernio may come handy in diagnosing the cause of otherwise undiagnosed ‘seronegative inflammatory polyarthritis’. Urticarial vasculitis can be suspected on typical skin lesions. Erythema nodosum and several other forms of inflammatory lesions of the subcutaneous tissue (panniculus) is seen in association with a number of inflammatory arthritides the best known being Lofgren syndrome (acute sarcoidosis), already mentioned above, Behcet's disease (the lesion often ulcerates) and IBD. Subcutaneous nodules in association with polyarthritis is seen with several diseases including RA, SLE, OA (Heberden’s and Bouchard’s nodules), gout (gouty
Approach to the Patient with Polyarthritis

tophi), sarcoidosis, rheumatic fever, polyarteritis nodosa, dislipidaemias, and others. Mucosal ulcers in SLE (moderately painful), SpA (little pain), and Behcet's disease (severely painful) are helpful clinical features for diagnosis. Palpable as well as non-palpable purpuric lesions are seen in several polyarthritides including SLE, Sjögren’s syndrome (including hypergammaglobulinaemic purpura of Waldenström) and others. Leg ulcers (vasculitic or part of neutrophilic dermatosis e.g. pyoderma gangrenosum) are seen in RA, SLE (subcutaneous inflammation that may ulcerate e.g. lupus profundus), polyarteritis nodosa (including cutaneous polyarteritis), Behcet’s disease and others. Keratoderma blenorhagicum seen with Reiter’s syndrome is a typical lesion that helps in making a definitive diagnosis. Recognition of gonococcal skin lesions could come in handy for diagnosing an otherwise idiopathic migratory inflammatory polyarthritis. Gross clubbing in a smoker presenting with painful swelling of distal joints in the extremities (wrists, small joints in the hands, ankles, joints in the feet) should immediately bring in the possibility of carcinoma lung-related hypertrophic pulmonary osteoarthropathy. The list is rather big to be covered here but suffice it would be to note that skin-subcutaneous tissue-mucosa (including nails, scalp) should be carefully evaluated in any patient with inflammatory polyarthritis.

The association of eye and ear-nose-throat-mouth with polyarthritis is possibly equally important. Sicca symptoms are well known features of Sjögren’s syndrome, but also occur secondary to RA, SLE, scleroderma and others. Episcleritis-scleritis is common in RA. Iridocyclitis-uveitis is typically seen in association with SpA group including Reiter’s syndrome. Retinal lesions are seen in SLE, systemic vasculitides and others, retrobulbar lesions (causing proptosis) may be seen in Wegener’s granulomatosis, involvement of rectus muscles may occur as part of inflammatory myositis. Inflammation of cartilage in the pinna and bridge of the nose (with similar cartilage lesions at other sites) is typically seen in relapsing polychondritis causing flail or deformed pinna giving the appearance of a ‘boxer’s ear’ and ‘saddle-nose’ deformity. The latter is also seen in Wegener’s granulomatosis that usually destroys the cartilage at bridge of the nose. Involvement of middle and inner ear is typically seen in Wegener’s granulomatosis.

Inflammatory polyarthritis also has close association with genitourinary and gastrointestinal
systems. Urethritic form of ‘reactive arthritis’, the most dramatic subset being Reiter’s syndrome, is a well known cause of seronegative inflammatory polyarthritis. Gonococcal infection with urethritis, cervicitis and migratory inflammatory polyarthritis is a well recognised association. IBD also has duel association with inflammatory polyarthritis. Thus, several patterns of inflammatory polyarthritis have been described in association with IBD including peripheral polyarthritis and erythema nodosum (mentioned above). Another form is that of spondyloartharthritis some of whom may evolve into frank ankylosing spondylitis. Subclinical / asymptomatic small segments of lesions of IBD have been demonstrated by endoscopic examination in a significant proportion of patients with spondyloarthritis [11]. Behcet’s disease is the other condition where IBD-type lesions may be seen. In fact, there are patients diagnosed as IBD who on detailed clinical evaluation may show features of milder forms of Behcet’s disease including oro-genital ulcers, erythema nodosum lesions, eye inflammation.

Renal disease and inflammatory polyarthritis combination is among the most serious, often life threatening forms of arthritic disorders. Urinary sediment abnormality indicative of glomerular inflammation (microscopic haematuria, variety of casts and WBC), sub-nephrotic or nephrotic range proteinuria, frank nephrotic syndrome, renal arterial involvement with renal hypertension, rapidly progressive glomerulonephritis, and end-stage renal disease are the manifestations of several diseases that may have associated inflammatory polyarthritis. This group mainly includes SLE and its overlap with other connective tissue diseases, antiphospholipid syndrome, and anti-neutrophil cytoplasmic antibody (ANCA)-associated systemic small and medium vessel vasculitides (Wegner’s granulomatosis, microscopic polyangiitis, Churg-Strauss syndrome) and classic polyarteritis nodosa. Peripheral as well as central nervous system involvement and inflammatory polyarthritis is another potentially serious, often life threatening group of arthritides. These include SLE, antiphospholipid syndrome, systemic vasculitides of several types (mononeuritis multiplex is a common manifestation in some of them), and Behcet’s disease. Lung involvement is commonly seen with RA, connective tissue diseases, systemic vasculitides, sarcoidosis, relapsing polychondritis, and AS. There is an important clinical subset of pulmonary-renal syndrome where kidney and lung are affected in addition to an inflammatory polyarthritis. SLE, scleroderma and other connective tissue diseases, ANCA-associated vasculitides, Goodpasture’s syndrome, pauciimmune necrotising and crescentic glomerulonephritis (CGN), Henoch-Schönlein’s purpura (HSP), and essential mixed cryoglobulinemia (EMC) are some of its causes [12]. Heart involvement is typically seen in anti-phospholipid syndrome, SLE, scleroderma, dermatomyositis, and in a form of systemic vasculitis seen in paediatric age group (Kawasaki disease). Rheumatic fever is too well know to be reminded of but, it must be noted that persistent inflammatory polyarthritis

Table 4: Commonly used nonspecific laboratory markers of inflammation (acute phase reactants)

1. Increased in:
   a. ESR
   b. Platelet count
   c. Total serum globulins with reversal of albumin/globulin ratio
   d. Leukocyte count (often but not always)
   e. CRP
   f. Alkaline phosphatase
2. Decreased in:
   a. Haemoglobin (normocytic normochromic anaemia of chronic disease)
   b. Serum albumin (with reversal of albumin/globulin ratio)
is not a feature of this disease. Moreover, it is a disease of paediatric age group. Polyserositis with inflammatory polyarthritis may be seen in SLE, overlap connective tissue diseases and a relatively uncommon condition in our country namely Familial Mediterranean Fever (FMF). Pleuropericarditis is typically seen in SLE but may be present in RA and other systemic conditions. Obstetric and gynaecological problems may occur in several diseases with inflammatory polyarthritis, mainly due to joint deformities causing biomechanical-physical issues. But, antiphospholipid syndrome is the most notorious for causing foetal wastage and related problems. Increased risk during pregnancy and purpura is characteristic of SLE. Haematological abnormalities are universal in inflammatory polyarthritis and include high erythrocyte sedimentation rate (ESR), high platelets, anaemia of chronic disease and occasionally, leukocytosis that could be extreme on occasions. However, some haematological abnormalities may specifically point towards a certain diagnosis. Thus, low platelets may point towards the diagnostic possibility of SLE and antiphospholipid syndrome. Rare cases of leukaemic arthropathies in adults may have not only low platelets but also other abnormalities in the blood that may be a clue to diagnosis. Hypercoagulable state with widespread thromboembolic manifestations is rather typical of antiphospholipid syndrome that is often associated with SLE.

**Joint Count**

It has been documented that formal quantitative joint count is not include in most visits of most patients with rheumatoid arthritis to most rheumatologists [13]. However, rheumatologists need to be reminded that with rapid advancements in drug therapy of patients with a variety of musculoskeletal diseases and especially that of inflammatory arthritides, some sort of objective assessment of the disease activity, the simplest method being joint count, must be carried out in every patient at the first encounter [14]. Irrespective of what methodology is adopted, it should not be ignored. One may try to adopt the most suited method for the type of clinical set-up one has. Original Disease Activity Score (DAS), its modification (DAS28), more recently devised and validated Clinical Disease Activity Index (CDAI) and Simplified Disease Activity Index (SDAI) are widely recommended for use in RA and other inflammatory arthritides [15]. Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Metrology Index (BASMI) are available for objective assessment of different aspects of inflammatory spinal arthritis. Methodology is also available for objective assessment of non-inflammatory diseases like osteoarthritis (e.g. WOMAC index). The importance of objective assessment of disease activity cannot be overemphasised. Over the years it has become clear that tight control of disease activity in inflammatory arthropathies prevents joint damage and disability and reduces morbidity and mortality. But, tight-control of disease activity is possible to achieve only if it is measured routinely. Treatment of diabetes mellitus or hypertension is good example to understand this argument. If blood glucose or blood pressure readings are not documented regularly they cannot be controlled satisfactorily. Unfortunately, most clinicians would treat inflammatory polyarthritis but, without knowing the degree of disease activity to guide them. Such a patient is likely to develop increasing damage and disability over time with increased morbidity and mortality.

**Investigations**

As mentioned above, the most crucial point towards making a diagnosis in polyarthritis is to differentiate between inflammatory and non-inflammatory conditions. History and physical examination provide good idea whether the condition is inflammatory in nature. In most situations the inflammatory nature of polyarthritis can be confirmed by routine laboratory investigations for non-specific markers of inflammation namely, raised levels of acute phase
proteins. Table 4 gives the list of commonly available tests for confirming inflammation. Some exceptions, however, must be pointed out. In certain diseases ESR may not truly reflect the inflammatory state. This is often true of SLE, scleroderma and AS where ESR may be disproportionately high or low. Similarly platelet counts may be low in SLE as part of its clinical manifestation, as also in a relatively uncommon condition in adults namely, leukaemic arthropathies. Examination of synovial fluid only to confirm inflammatory nature of the joint disease is generally not recommended as this can be reasonably suspected on history and physical examination and confirmed by tests for acute phase reactants. However, on rare occasions there could be some confusion because of poor history, no definite clue in physical examination and inconclusive or border-line results of acute phase reactants. In such cases joint fluid examination (if joints have effusion) for leukocyte count can help. A leukocyte count of > 2000/cmm is a definite sign of inflammatory synovitis. Additional tests including gram-staining, bacterial and mycobacterial culture, and examination under polarised light microscopy for crystals would also help in making a definitive diagnosis. Radiological examination of the joints and other routine imaging investigations do not distinguish between inflammatory and noninflammatory conditions. They may, however, detect typical pattern of radiological abnormalities associated with certain diseases (e.g. typical erosions of RA or PsA in feet and hand joints, typical ‘scooped-out’ lesion of chronic gouty joint, sacroiliitis of SpA, aggressive destructive lesions of joint tuberculosis and other infections, chondrocalcinosis in calcium pyrophosphate dihydrate {CPPD} crystal deposition disease, etc.). This may indirectly give a clue to the inflammatory nature of the joint disease. Magnetic resonance imaging (MRI) on the other hand can demonstrate bone marrow oedema that has been demonstrated to be the earliest sign of inflammatory nature of the joint disease in recent studies [16]. Being an expensive investigation it cannot be recommended for routine use for confirming inflammatory joint disease. Histopathology is another investigation that may give a definitive diagnosis in difficult cases of polyarthritis. However, only in rare circumstances synovial biopsy may be necessary for making a diagnosis. Thus, it may be required in suspected polyarticular infection (mycobacterial infection, fungal), villonodular synovitis etc. On the other hand skin or subcutaneous lesions may often yield useful diagnostic information (e.g. sarcoidosis, erythema nodosum, vasculitis). Specific tissue biopsy may be indicated in specific diseases e.g. sural nerve biopsy in systemic vasculitis, muscle biopsy in inflammatory myositis.

Once a provisional diagnosis has been made, in the second-step of diagnostic work-up, more specific investigations are usually required. Thus, in RA, one may like to have some idea of disease prognosis. Quantitative measurement of rheumatoid factor (RF) and anti-CCP antibody are useful in this respect. In suspected SLE and related connective tissue disorders screening for immunofluorescent antinuclear antibody (F-ANA) is of great importance. F-ANA has a very high sensitivity for SLE and other connective tissue diseases but it has rather low specificity. This makes F-ANA a very useful test for excluding the diagnosis of these diseases; if F-ANA test is negative it would be most unlikely that the patient would have SLE or related connective tissue disease. Immunofluorescent anti-neutrophil cytoplasmic antibody (ANCA) test is similarly a very useful screening test for patients suspected of systemic vasculitides; a negative immunofluorescent ANCA test would go strongly against the diagnosis of ANCA-associated vasculitides. ANCA titres have also been shown to have some degree of correlation with disease activity. For routine monitoring of drug toxicities standard complete blood counts, liver enzymes, renal parameters, and routine urine examination would suffice in most cases. Baseline electrocardiogram, chest radiograph and stool examination (including occult blood) should be done routinely in patients with polyarthritis. HLA B27 screening is very useful but only in a patient with typical history of inflammatory back pain, its presence
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would be strongly favour the diagnosis of ankylosing spondylitis.

Non-Specific Arthralgias, Myalgias, Pain Amplification Versus Polyarthritis

There are patients who present with vague pains in the joints, muscles and other parts of the musculoskeletal system. They may also complain of developing numbness in different parts of the extremities on inactivity, neck-nape region pains, pains running down from neck along the arms, low back pain that often runs down along the legs. Usually the severity of the pain fluctuates and is often described as ‘unbearable’. They may show features of anxiety, fear of ‘getting crippled over time’, or worry about some serious unrecognised disease. They often have sleep abnormalities (‘I am as tired on getting up in the morning as I am when I go to bed’) often associated with some features of fibromyalgia including fibromyalgic tender spots. In most cases the duration of symptom is vaguely ‘since long’ and they carry bags-full of investigation and imaging reports. They usually have a ready-made hand written list of complaints (‘I have written it down lest I forget some of them when I visit the doctor’) and another list of specialists they have already consulted (‘I have already consulted so-and-so’, usually a list of famous doctors from ‘Who-is-who’ list), yet they have not been satisfied as no definite diagnosis has been made and their symptoms are getting worse. They continue to remain worried and frustrated. This is a most puzzling group who should not be over diagnosed or over treated as if they had a disease. Occasionally they may be mistaken as having true polyarthritis and started on some form of ‘arthritis treatment’. This approach of management must be strongly discouraged as it leads to psychological dependence on such treatment. Once a label of ‘arthritis’ is put on such patients it becomes almost impossible to convince them later that they do not have ‘arthritis’. However, a complete evaluation is called for in older age persons, in those with disease of more than 6 weeks duration, and in those with constitutional symptoms or symptoms referable to other organ systems. A limited evaluation should include careful history, review of systems, physical examination and minimal investigations including non-specific markers of inflammation (ESR, high sensitivity-C-reactive protein [hs-CRP]), test for thyroid status (minimum thyroid stimulating hormone [TSH]levels TSH), anti-CCP antibodies, and routine cancer screening (chest x-ray, prostate specific antigen, mammography, stool occult blood), if these had not already been done in the recent past. In most such cases the problem usually turns out to be functional and related to pain amplification. It is best to address their concerns directly in a forthright manner. Some of them may require help of a counsellor or a psychiatrist. Table 1 gives some of the mimics of polyarthritis.

Table 1

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<th>Mimics of Polyarthritis</th>
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<tr>
<td>Arthritis mimics</td>
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<tr>
<td>Rheumatoid Arthritis</td>
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<tr>
<td>Psoriatic Arthritis</td>
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<tr>
<td>Gout</td>
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<tr>
<td>Lateral Epicondylitis</td>
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<td>Tendinitis</td>
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<tr>
<td>Myofascial Pain</td>
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<td>Fibromyalgia</td>
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Summary

As a general rule, in musculoskeletal diseases 80% of the information towards making a diagnosis comes from accurate clinical history, 15% from physical examination and only 5% from laboratory investigations. The same rule holds true for patients with polyarthritis. Polyarthritis and its diagnosis encompass almost the whole field of rheumatology. Making a diagnosis of polyarthritis is really a test of the knowledge of general internal medicine; deeper the knowledge of general internal medicine easier it is for the clinical rheumatologist to reach a definitive diagnosis. Polyarthritis is among the commonest problems that a rheumatologist faces in his/her daily practice, it is necessary to follow a definite diagnostic algorithm for convenience and accuracy. Is it polyarthritis? → What is the duration (acute or chronic)? → What are the circumstances of onset? → Is it inflammatory or non-inflammatory? → What is the pattern of evolution? → What is the topography of involvement? → Is there a clue to diagnosis in the past history, family history and review of systems? → Does physical examination give a diagnostic clue (e.g. a small psoriatic patch)? This approach
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narrow down the diagnostic possibilities and helps in requisitioning a limited number of focused relevant investigations to confirm the diagnosis. In the majority, specific drug treatment along with patient education, counselling, occupational and physiotherapy may be initiated even before all the investigation reports become available. However, in doubtful cases it would be prudent to initiate only symptomatic treatment till all the relevant reports become available to make a definitive diagnosis. Acute inflammatory polyarthritis could be a self limiting benign condition, the beginning of a serious chronic illness with significant morbidity that could even be life threatening or, a rheumatological emergency requiring urgent diagnosis and management. Distinction between benign, serious chronic illness and a rheumatological emergency requires deep knowledge of rheumatology as well as general internal medicine; details of past, family and personal history and in-depth review of systems, usually help reaching a working diagnosis. Addition of a few relevant investigations usually confirms the diagnosis that helps in initiating appropriate treatment.

Key Points: Approach to the patient with polyarthritis

- True Polyarthritis vs. Polyarthralgia or non-specific MSK pains
  - Pattern of evolution:
    - Intermittent vs. migratory vs. additive
  - Disease duration
    - Acute vs. Chronic
- Pathological nature of the disease
  - Inflammatory vs. Non-inflammatory
- Pattern (topography) of joint involvement
  - Peripheral vs. axial disease
  - Overlap peripheral and axial involvement
- Peripheral arthritis
  - Symmetrical vs. asymmetrical
  - Upper vs. lower segment predominantly involved vs. equally involved
  - Without vs. with axial involvement
- Unique patterns
  - Purely DIP (Inflammatory: psoriatic arthritis, sarcoidosis, IBD-related; Non-inflammatory: Nodular primary OA)
  - Peri-ankle / ankle inflammatory arthritis with erythema nodosum and hilar lymphadenopathy (Lofgren syndrome)

References


13. Pincus T, Segurado OG. Most visits of most patients with rheumatoid arthritis to most rheumatologists do not include a formal quantitative joint count. Ann Rheum Dis 2006; 65: 820-2.


