Dear Colleagues

Hope you enjoyed the May issue of MoveS.

As we suggested earlier we are striving to go green and hoped to do so by this issue. We had some protests though and are hoping to convince the stragglers to go ahead and get e-connected so that they can be easily contacted, benefit from the news letters and also help us to conserve the trees!! This issue is a dual one: e and paper both. Please co-operate friends and mail your e-mail ids to either Rashna or me at rashnadass@gmail.com / drsujatasawhney@gmail.com.

So please, help us and join the e-journey that we would like to share with you….

Our first issue helped you to decide which patients need to be referred to a pediatric rheumatologist and also why JIA patients deserve an early diagnosis.

This issue focuses on “An approach to a child with arthritis”

It is baffling that orthopedic surgeons see children with arthritis in this country. It is well proven that children who are not referred to a pediatric rheumatologist are often subjected to unnecessary procedures and have a significant delay to their diagnosis. It is hoped that this issue will give you an insight into the causes of arthritis in children and help us all to reverse this trend!!

Dr Raju Khubchandani from Mumbai is organizing a week’s intensive training programme at the Jaslok Hospital in September that is being attended by international delegates in addition to our local pediatricians. Congratulations Dr Khubchandani! I am sure that this will go a long way in helping the children with rheumatologic problems in our country.

Dr Nandani Bhabulkar is the organizing secretary for the Pediatric Rheumatology Annual Conference at Nagpur this year: November 2009. Please spread the message and help her to make the conference a success. Details are in the newsletter.

Happy Reading!

The editorial team
Dr Sujata Sawhney, New Delhi
Dr Rashna Dass, Shillong
Childhood arthritis is a common problem with a multitude of differential diagnosis. Parents usually seek help of paediatrician/orthopaedic surgeon for a child who is limping, has a swelling in one or more joints or less commonly complaining of pain without any obvious swelling.

Arthritis in children can present as acute or chronic, monoarticular or polyarticular, with or without constitutional features. The differential diagnosis of various presentations is varied and is a source of constant dilemma to the attending physician.

For the sake of simplicity the various presentations of childhood arthritis are dealt with in separate parts.

**APPROACH TO ACUTE MONOARTICULAR ARTHRITIS**

An acutely painful joint is an emergency and needs to be diagnosed at the earliest not only to alleviate pain but also to prevent damage to the joint.

A detailed history and thorough clinical examination go a long way in narrowing down the diagnosis. Radiography along with laboratory support helps in the confirmation of the diagnosis.

**History**

The age of the patient, the type of onset and the presence or absence of constitutional features help in narrowing down the wide differential in these children.

**Age:**

- Neonates: A neonate presenting with an acutely swollen joint can have septic arthritis, NOMID (Neonatal Onset Multi Inflammatory Disease), developmental dysplasia of hip
- Infants: Septic arthritis, Hemarthrosis due to bleeding disorders like haemophilia presents in infancy especially when the child is weight bearing, developmental dysplasia of hip mild variant
- Childhood: Septic arthritis, trauma, mechanical derangements, hypermobility, infiltrative disorders, reactive arthritis, juvenile idiopathic arthritis, skeletal dysplasia etc. usually present in childhood

**Onset:**

- Sudden: Sudden onset swelling and pain developing over minutes to hours is usually indicative of trauma causing fracture or soft tissue injury
- Acute: Pain and swelling of a joint over hours to days is suggestive of septic joint, reactive arthritis, Hemarthrosis, acute rheumatic fever etc.

**Constitutional features:** Presence of fever, sore throat, weight loss, loss of appetite, diarrhoea, dysentery, urethral discharge, history suggestive of uveitis, oral mucosal ulcers, hair fall, rash over skin etc. is to be inquired for

**Nature of pain:**

- Is the pain severe enough to disturb the sleep of the child? (Osteomas)
- Is there any early morning stiffness? (Inflammatory)
- Does the pain worsen after movement or does it get worse with exercise? (Inflammatory vs. Mechanical)

**Site and distribution of pain:** In childhood arthritis recognition of the pattern of pain is very important as majority of the illnesses follow a pattern of joint involvement which aids the diagnosis.

To interpret the pattern correctly it is necessary to know the following:

- Where did the pain start from?
- Which joints are involved?
- Upper limb joints/lower limb joints
- What is order of involvement?
- Whether arthritis is migratory or non migratory?
- Is the joint involvement symmetrical or asymmetrical?
- Is joint pain part of a systemic illness?

**Associated medical illnesses:** Psoriasis, Inflammatory bowel disease, tuberculosis etc.

**Drug history:** Long term steroids can cause avascular necrosis, retinoids, anticonvulsants can unmask or exacerbate the articular manifestations of lupus

**Family history:** History of arthritis, psoriasis

**Examination**

**General examination:** Complete head to toe examination is required.

- Weight and height should be taken and growth charted if previous records available
- Look for alopecia, pallor, redness of eyes, cataract, icterus, rash, lymphadenopathy, nail pitting, thickening of skin, pigmentation, psoriasis, oral ulcers, nodules, raynaud’s phenomenon etc.

**Systemic examination:**

- CVS: Heart rate, murmurs
- Abdominal examination: Visceromegaly
- Respiratory System: Dyspnoea, intercostals retraction etc.
- CNS: Headaches, neuropsychiatric manifestations (pointing towards SLE) need to be ruled out

**Local examination:**

- Inspection: Warmth, Swelling, Redness
  - Look for soft tissue swelling
Examination: Movements of the joint
 ascending whether the swelling is articular or periarticular

Sometimes the swelling and pain might be in the surrounding soft tissues in osteomyelitis and the joint is normal. Joint movements give a clue to this. Passive movements are possible in periarticular conditions vis a vis articular conditions where passive movements are restricted

Enthesitis is to be ruled out by examination of the entheses especially the Tendo Achilles

Laboratory markers:
- Complete blood count, ESR, CRP, Blood culture, ANA, ASO titre, throat swab
- Ancillary investigations for specific diagnosis like Hb electrophoresis for sickle cell disease, factor VIII and factor IX estimation for hemophilia.
- Synovial fluid examination:

  - Synovial fluid aspiration: Most important investigation. Should be done by an experienced person with all aseptic precautions. On the basis of synovial fluid aspiration the diagnosis can be divided into three broad categories, first the fluid can be hemorrhagic and the diagnosis is either hemorrhagic or pigmented villous nodular synovitis. If the cell count in the synovial fluid is between 1500 cells/mm³ to <50,000 cells/mm³, it is suggestive of inflammatory/reactive arthritis. If the cell count is more than 50,000 cells/mm³ it is indicative of septic arthritis. Synovial fluid culture can help identify the specific organism and the sensitive antibiotic can be given.
- Radiography: X-Ray of the joint affected, MRI, Bone scan. CT scan or MRI are increasingly being used to identify the cause of an acute monoarthritis specially after history of trauma or where the pattern of joint involvement is suggestive of JIA eg an eight year old male patient presenting with knee effusion and Tendo Achilles swelling, where MRI becomes the investigation of choice to document tendinitis

for the diagnosis of Enthesitis related arthritis. MRI is also helpful in the early diagnosis as it picks up bone edema early on in the disease course which is a sensitive marker for an inflammatory process

Figure 1 Algorithm for acute monoarthritis

<table>
<thead>
<tr>
<th>Sick child</th>
<th>Well child</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>H/o significant trauma</td>
</tr>
<tr>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Septic arthritis</td>
<td>Partially treated sepsis</td>
</tr>
<tr>
<td>Reactive arthritis</td>
<td>Malignancy</td>
</tr>
<tr>
<td>Kawasaki disease</td>
<td>Connective tissue disorders</td>
</tr>
<tr>
<td>Malignancy</td>
<td>Fractures</td>
</tr>
<tr>
<td>Sickle cell disease</td>
<td>Mechanical derangements</td>
</tr>
<tr>
<td>JIA</td>
<td>Bleeding disorders</td>
</tr>
<tr>
<td>DDH</td>
<td>Neoplasias</td>
</tr>
<tr>
<td>Osteochondroses</td>
<td>JIA</td>
</tr>
<tr>
<td>Slipped capital epiphysis</td>
<td></td>
</tr>
</tbody>
</table>

Table 1. Differential diagnosis of acute monoarticular arthritis

- Septic arthritis
- Reactive arthritis: most common
  - Post streptococcal reactive arthritis
  - Poncet’s disease
- Trauma
- Foreign body synovitis
- Hemarthrosis
  - Trauma
  - Haemophilia
  - Haemangioma
  - Pigmented villous nodular synovitis
- Infections
  - Lyme disease
  - Acute gonococcal arthritis
- Neoplastic diseases
  - Acute leukemia
  - Lymphomas
  - Neuroblastomas
  - Osteoid osteoma
- JIA
  - Systemic onset
  - Psoriatic arthritis
  - Enthesitis related arthritis
- Connective tissue disorders
  - SLE
  - Juvenile dermatomyositis
  - Vasculitides: HSP

Treatment

According to the diagnosis, treatment is to be instituted. Broad spectrum antibiotics can be started till specific organism is isolated from a septic joint.

NSAIDs can be given to alleviate pain and to decrease inflammation. Surgical correction or plaster cast may be necessary for a mechanical derangement

Figure 1 Acutely swollen joint
## APPROACH TO CHRONIC MONOARTHRITIS

Arthritis for more than 14 days is termed as chronic.

### History

**Onset:** Usually insidious, sometimes a partially treated acute septic joint can present as a chronic arthritis.

**Pattern:** In chronic monoarthritis recognition of the pattern of joint involvement is very important, e.g., in oligoarticular JIA, patient presents with few or absent constitutional symptoms and swelling or limitation of movement is often noted by parents. It is usually asymmetrical. A bilaterally symmetrical joint involvement is less common and is more in favour of a reactive arthritis.

**Constitutional symptoms:** Fever, rash, lymphadenopathy etc. are present in systemic onset JIA, SLE and other connective tissue disorders. Arthritis in a child with juvenile dermatomyositis is associated with proximal myopathy and rash.

**Nature of pain:** Migratory as in Acute rheumatic fever, relapsing as in Hemarthrosis.

**Duration:** In chronic arthritis, duration of joint swelling is important as most diseases have a vertical presentation in children. The time period for classification of JIA and reactive arthritis is 6 weeks. If a child is suspected to be having oligoarticular JIA then a time period of 6 weeks should elapse before labelling the disease as other differentials like post streptococcal reactive arthritis would usually subside by 6-8 weeks.

**Past history:** History of a joint swelling or of any illness like sore throat, diarrhoea, dysentery recently (8 weeks), old trauma leading to mechanical derangement needs to be inquired about.

### Algorithm for Chronic Monoarthritis

<table>
<thead>
<tr>
<th>Sick child</th>
<th>Well child</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partially treated septic arthritis</td>
<td>↓</td>
</tr>
<tr>
<td>TB</td>
<td>Oligoarticular JIA</td>
</tr>
<tr>
<td>Reactive arthritis</td>
<td>Enthesitis related arthritis</td>
</tr>
<tr>
<td>Systemic onset JIA</td>
<td>Psoriatic arthritis</td>
</tr>
<tr>
<td>Vasculitides</td>
<td>Pigmented villous nodular synovitis</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>Mucopolysaccharidoses</td>
</tr>
<tr>
<td>SLE</td>
<td>Mechanical</td>
</tr>
<tr>
<td>Connective tissue disorders</td>
<td>Plant thorn synovitis</td>
</tr>
<tr>
<td>Infiltrative diseases</td>
<td></td>
</tr>
</tbody>
</table>

### Figure 2. Psoriatic rash

### Figure 3. Corneal opacity with untreated uveitis

### Table 2. Differential Diagnosis of Chronic Monoarthritis

- **Infection associated**
  - Partially treated septic arthritis
  - Post infectious arthritis
  - Fungal
  - Viral
  - Reactive arthritis
  - Tubercular arthritis

- **Psoriatic arthritis**

- **Vasculitides**
  - HSP

- **Connective tissue disorders**
  - SLE
  - Plant thorn synovitis
  - Pigmented villous nodular synovitis
  - Mucopolysaccharidoses

- **Mechanical**
  - Chondromalacia patellae

- **Periodic fever syndromes**

- **Hemophilic arthropathy**

- **Celiac disease**

### Investigations:

Laboratory tests: Complete blood count, ESR, CRP, Blood culture, Quantiferon test, Mantoux test, screen for celiac disease if suspected, PT, aPTT etc. according to the clinical diagnosis.
**Imaging:** Forms the backbone of the diagnosis. Plain X-ray of the affected joint with the contralateral joint as control usually gives the clue to the diagnosis. MRI is superior to CT scan for the diagnosis as bone edema can be picked up earlier. Sometimes a bone scan is required to identify osteomyelitis, non bacterial osteitis or bone infiltration.

**Treatment:** Specific according to diagnosis

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**APPROACH TO POLYARTHRITIS**

Polyarthritis is defined as involvement of more than one joint.

Joint involvement lasting less than 6 weeks is termed as acute polyarthritis

Joint involvement lasting beyond 6 weeks is chronic polyarthritis

**History**

**Onset:** Polyarthritis can present with joint pains preceding constitutional symptoms or more commonly with fever and other constitutional symptoms presenting prior to onset of joint involvement.

**Pattern:** Recognition of joint involvement is imperative for the diagnosis e.g. migratory or fleeting joint pain with fever preceded by sore throat is suggestive of acute rheumatic fever, additive pattern where some joints are involved at first and persist with recruitment of more joints later e.g. polyarticular SLE.

**Inflammatory vs non inflammatory:** Pain in various joints due to hypermobility is non inflammatory as it appears at any time of day, (usually in the evenings after a day of hectic activity), is not associated with early morning stiffness and worsens with activity. On the contrary, inflammatory polyarthritis is worse in morning and improves with gentle activity.

Constitutional symptoms: History of irritable bowel, fever, redness of eyes, sore throat, rash, photosensitivity, early morning stiffness, oral ulcers, alopecia etc. is to be inquired for by direct questioning.

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**Fig. 4 Acute Inflammation of the eye**

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**Fig. 5 Multiple swollen joints**

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**Table:**

<table>
<thead>
<tr>
<th>Type of Disease</th>
<th>Duration</th>
<th>Affected Joints</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral arthritis</td>
<td>&lt;6weeks</td>
<td>&lt;6weeks</td>
</tr>
<tr>
<td>SOJIA</td>
<td>&gt;6weeks</td>
<td>&gt;6weeks</td>
</tr>
<tr>
<td>HSP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polyarticular JIA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infectious endocarditis</td>
<td>TB</td>
<td>Kawasaki disease</td>
</tr>
<tr>
<td>Acute rheumatic fever</td>
<td>HIV</td>
<td>Post streptococcal reactive arthritis</td>
</tr>
<tr>
<td>Cold scratch disease</td>
<td>SLE</td>
<td>Sickle cell anemia</td>
</tr>
<tr>
<td>Lyme disease</td>
<td>JDM</td>
<td>Psoriatic arthritis</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>Reactive arthritis</td>
<td>Metabolic disorders</td>
</tr>
<tr>
<td>Salmonellosis</td>
<td>PAN</td>
<td>Mechanical</td>
</tr>
<tr>
<td>Reiter’s Syndrome</td>
<td>Infiltrative diseases</td>
<td>Genetic</td>
</tr>
<tr>
<td>Kawasaki disease</td>
<td>IBD assoc arthritis</td>
<td>Mimics</td>
</tr>
</tbody>
</table>

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**Fig. 6 Dactylitis**
Table 3. Differential Diagnosis for Polyarticular arthritis with Fever

Infections
- Acute Rheumatic Fever
- Infectious endocarditis
- Lyme Disease
- Cat Scratch disease
- Salmonellosis
- Sarcoidosis
- TB
- HIV
- Hepatitis B

Reactive arthritis
- Reiter’s complex

Systemic onset JIA

IBD associated arthritis

Vasculitides
- Kawasaki disease
- Polyarteritis nodosa

Sickle cell crisis

Malignancy
- ALL
- Neuroblastoma

Management

Investigations: Diagnosis of Juvenile idiopathic arthritis is a diagnosis of exclusion and a plethora of clinical conditions need to be ruled out before reaching a conclusion.

Clinical examination and history taking help in forming a diagnosis and the laboratory markers and imaging confirm or corroborate the clinical suspicion.

Tests to rule out common infections like TB need to be done. Complete blood count, ESR, CRP, Sr.Ferritin give a general view of infections/inflammation. HIV and hepatitis should be ruled out. Specific tests like ANA, RF, Anti CCP antibody and HLA B 27 are done when autoimmune disorders are suspected.

Imaging: Important to find out the exact pathology. Plain radiographs are valuable specially to rule out the mimics of JIA. MRI of the affected joints is required sometimes when there is a strong clinical suspicion of a joint involvement but signs and symptoms are few or masked by concomitant use of anti inflammatory drugs.

Endoscopy of the lower GI tract is done to rule out colitis if there is history suggestive of the same.

Treatment: Specific therapy is instituted after the diagnosis.

Table 4. Differential diagnosis of Polyarthritis without fever

Polyarticular JIA
- Seronegative
- Seropositive

Enthesitis related arthritis

Inflammatory bowel disease associated arthritis

Psoriatic arthritis

Infections
- Lyme disease
- HIV
- TB
- Gonococcal arthritis
- Parvovirus B19

Connective Tissue disorders
- SLE
- Juvenile Dermatomyositis
- Scleroderma

Sickle cell dactylitis

Mucopolysaccharidoses
- Morquio’s
- Scheie

Malignancy
- Neuroblastoma

Vasculitides
- HSP

Metabolic disorders
- Gaucher’s
- Fabry’s
- Diabetic cheiroarthopathy

Mechanical
- Ehlers Danlos syndrome
- Benign joint hypermobility

Genetic
- Winchester Syndrome

Mimics
- Pseudo rheumatic dysplasia
- Skeletal dysplasia
- Spondyloepiphysyal dysplasia
Conclusion

Managing a case of arthritis for a paediatric rheumatologist is akin to a paediatrician managing a case of fever. History gives 85% information, examination adds 10% and the laboratory support aids in the last 5%. An unwell febrile child with an acutely painful joint is a medical emergency as it is critical to diagnose septic arthritis to prevent joint damage in the long term. Most other diseases take time to manifest the full form and be identified. It is often impossible to be certain of the diagnosis on first contact with many patients. It is important to:

- Identify the underlying disease
- Avoid hasty use of NSAID/steroid without establishing the diagnosis as the clinical picture is obscured
- Seek help from a paediatric rheumatologist where the need arises.

VII
NATIONAL CONFERENCE OF
PEDIATRIC RHEUMATOLOGY
7th & 8th November, 2009
Nagpur, India

Organised By
Indian Academy of Pediatrics,
Nagpur Branch
Division of Pediatric Rheumatology,
Singla Hospital & Research Centre
IAP-Rheumatology
Chapter

Co-Hosted by

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Lets join hands to take care of young Joints
Controlling JIA can help your pediatric patients get out and play

Enbrel was the first biologic indicated for JIA

Rapid and sustained response in pediatric patients taking ENBREL

- Rapid response at 1 month – sustained in pediatric patients taking Enbrel
- > 90% reduction in median active joint count at 4 years

ENBREL offers an established safety profile in JIA

Studied in patients from 4 to 17 years of age
- In general, the adverse events in JIA patients were similar in frequency and type to those seen in adult RA patients
- No deaths or malignancies were reported during 5 years of treatment in ENBREL patients with JIA

Dosage: Juvenile Rheumatoid Arthritis Patients: 0.4 mg/kg (up to a maximum of 25 mg per dose) twice weekly as a subcutaneous injection 72-96 hours apart

Balancing Risk Information

Serious infections, including tuberculosis, and sepsis have been reported. Some of these infections have been fatal. Do not start ENBREL in the presence of allergy to ENBREL or its components. Rare cases of progressive multifocal leukoencephalopathy, although the causal relationship to Enbrel remains unclear. Rare cases of pancytopenia, and very rare cases of aplastic anemia, some fatal, have been reported in patients treated with ENBREL. Exercise caution in patients who have a previous history of significant hematologic abnormalities. Reports of malignancies occurring in various sites have been received in the postmarketing period. Effects of ENBREL therapy on the development of cancer are unknown. In clinical trials of TNF antagonists, rare cases of lymphoma were seen compared to control patients; however, the risk of lymphoma may be higher in JIA patients.

Before initiation of therapy with ENBREL, any patient at increased risk for tuberculosis (TB) should be evaluated for active or latent infection. Prophylaxis of latent TB infection should be initiated prior to therapy with ENBREL. Applicable local guidelines should be consulted. Reactivation of hepatitis B virus (HBV) in patients who are chronic carriers of this virus who are receiving anti-TNF agents, including ENBREL, has been reported. Patients at risk for HBV infection should be evaluated for prior evidence of the virus before initiating anti-TNF therapy. Although a causal relationship has not been established for ENBREL, caution should be exercised when administering ENBREL to patients identified as carriers for HBV.

References:
1. ENBREL Summary of Product Characteristics, Wyeth Pharmaceuticals.
3. Remicade Summary of Product Characteristics, Centocor B.V.
5. Uremia Summary of Product Characteristics, Bristol-Myers Squibb Pharmaceuticals.

Full Prescribing Information Available on request through Wyeth Limited, RSC, Mahindra Towers, 4th Floor, A-wing, Dr. G.M. Bhausal Road, P.O. Box 6665, Worli, Mumbai 400 018, India
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