

# Paediatric Arthritides

**Roux P**, MBChB, M Phil(Bioethics), MD, DCH, FCP(Paed)

**Rainier-Pope C**, MBChB, MMed(Paed), DCH

**Power M**, BSc(Hons), MBBCh, MD

Department of Paediatrics and Child Health

Faculty of Health Sciences

University of Cape Town

**Correspondence:** Dr Paul Roux, PO Box 13657, Mowbray, 7705  
Tel (021) 404 3020, Fax (021) 406 6169, e-mail: proux@uctgsh1.uct.ac.za

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## Introduction

Children with joint disease frequently present with relatively non-specific symptoms, such as aches, limps, pains in joints and limbs, fever and rashes. Correct diagnosis rests on the careful interpretation of symptoms and signs and a knowledgeable understanding of the differential diagnosis.

Rheumatic conditions – those joint diseases mediated by autoimmune-induced inflammatory changes – tend to be chronic or recurrent. The time required to make a correct diagnosis of these conditions provides space to rule out infectious causes of arthritis, to investigate the child for other potentially serious conditions and to identify those children with amplified pain syndromes who have found their way to the rheumatology clinic.

## Differential diagnosis

Table I summarises the conditions most frequently presenting with a syndrome that includes arthritis, or symptoms that simulate arthritis. Conditions are classified according to the rate with which symptoms appear and the number of joints most frequently involved in each condition.

A child with joint symptoms, 'toxicity' and a swinging fever should be investigated for hidden sepsis.

Chronic infection, such as from malaria, tuberculosis and HIV/AIDS, may present with a disease syndrome that overlaps that of rheumatoid

arthritis. Underlying malignancy should be ruled out, particularly when bone pain – which tends to be worse at night – might be masquerading as joint pain.

## Infectious and post-infectious arthritis

Children with *septic arthritis* are usually very ill, with high fever and a hot, swollen joint with a markedly restricted range of movement. The diagnosis is made by aspiration of the joint or by the clinical syndrome and a positive blood culture.

*Tuberculous infection* of a joint must be ruled out by biopsy in any persistent mono-arthritis.

*Reactive (or post-infectious) arthritis* is common in children. It is defined as a non-suppurative arthritis

**Figure 1:** Monoarthritis due to juvenile idiopathic arthritis (JIA)



**Table I:** Monoarthritis of acute onset

Condition	Supportive evidence
Septic arthritis	Pus from joint space for bacterial culture
Malignancy	Bone pain near joint, often worse at night
Trauma	History
Non-accidental injury	Story and findings are discordant
Haemophilia	Boy, other evidence of bleeding disorder
Slipped upper femoral epiphysis	Adolescent, often obese, acute atraumatic onset
Reactive arthritis	Prior infection, often streptococcal
Pauci-articular onset juvenile idiopathic arthritis	Rarely presents with acute onset. Retrospective diagnosis
Spondylo-arthropathy	More often boys, nearing their second decade
Osteochondritis	
Osteonecrosis (including Perthes')	
Idiopathic osteolysis of the hip	

**Table II:** Monoarthritis of gradual onset (chronic)

Condition	Supportive evidence
Pauci-articular onset juvenile idiopathic arthritis	Preschool girl, develops further joint involvement later
Spondylo-arthropathy	Back pain becomes part of the picture
Tuberculosis	Other evidence of TB, biopsy and culture
Other conditions	Usually need biopsy and culture to diagnose

**Table III: Polyarthritis**

Condition	Supportive evidence
Acute rheumatic fever	Follow modified Jones criteria (post-streptococcal infection)
Reactive arthritis	Recent infection of any sort (rheumatic fever now regarded as a reactive arthritis)
Juvenile idiopathic arthritis	Often symmetrical, initially non-erosive arthritis, of large and small joints
Spondylo-arthritis	Back pain and enthesitis
Systemic lupus erythematosus	Skin changes, other organs involved
Osteochondritis/osteneclerosis (including Perthes' and avascular necrosis)	Better after rest, worse with exercise
Slipped upper femoral epiphyses	Adolescent, obese, acute onset, atraumatic
Other conditions	Biopsy required

**Figure 2: Polyarthritis due to juvenile idiopathic arthritis (JIA)**



that occurs in close temporal association with a non-articular infection. A history of sore throat, a positive throat swab for  $\beta$ -haemolytic streptococcus, an elevated anti-streptolysin-O titre (ASOT), or an elevated anti-DNAse B titre may provide evidence of a recent streptococcal infection.

*Acute rheumatic fever* (ARF) follows infection with a group A  $\beta$ -haemolytic streptococcus. The characteristic flitting nature of the arthritis is most useful in distinguishing acute rheumatic fever from rheumatoid arthritis. Joint symptoms are seldom predominant for long. The modified Jones Criteria are important. Absence of an elevated ASOT almost rules out ARF. Once acute rheumatic fever has been ruled out, the other reactive and post-infectious arthritides can be treated symptomatically with non-steroidal anti-inflammatory drugs. The patient should be followed up to ensure that the signs and symptoms of arthritis resolve within three months.

**Mechanical disorders**

Symptoms in mechanical disorders, such as *avascular necrosis*,

*osteochondritis* and *overuse tenosynovitis*, are usually related to physical activity and are more common in adolescents. In contrast to inflammatory joint disease, the symptoms tend to worsen during the course of the day. The knee, ankle, hip and back are most commonly involved. The *hypermobility syndrome* is an extreme variation of normal. It may be associated with mild recurrent arthritis and may predispose to injury, but the prognosis is good. It is more frequent in girl gymnasts and ballet dancers.

The diagnosis of hypermobility syndrome requires the presence of at least three of the following:  
 1. The thumb can be opposed to the flexor aspect of the forearm.

2. The fingers can be hyper-extended to parallel with the extensor aspect of the forearm.
3. Elbows or knees can be hyper-extended by at least 10 degrees.
4. There may be excessive ability to dorsiflex the ankle and to eversion of the foot.

**Non-accidental injury**

Acute joint swelling from non-accidental injury may result from traumatic periostitis, haemorrhage or fractures of the epiphysis. If the presenting history does not fit with the findings on examination, non-accidental injury should be considered. A more detailed history should be sought and a radiographic skeletal survey and/or bone scan should be considered.

**Amplified pain syndromes**

The discomfort of amplified pain syndromes is real. These children present with a history of pain, which may be severely disabling. Examination of the joints and special investigations reveal no evidence of inflammation.

**Figure 3: Hypermobility of joints**



**Fibromyalgia** is characterised by diffuse, often ill-defined musculoskeletal aching and stiffness, and multiple tender points in characteristic locations. Sleep is disturbed and the patient is often anxious and depressed. The erythrocyte sedimentation rate, platelet count and C-reactive protein

titre are normal. The syndrome is well recognised in adults. It occurs in adolescent girls, but is rare in boys.

Treatment is difficult. Parents and patient should be reassured that, although the pain is real, there is no underlying serious disorder. Physiotherapy, paracetamol or non-steroidal anti-inflammatory drugs (NSAIDs) and low-dose tri-cyclic antidepressants (e.g. amitriptyline 10 mg nocte) may be offered.

**Figure 4:** Gottron's papules - skin lesions associated with dermatomyositis



**Figure 5:** Malar rash and palatal lesions in SLE



### Growing pains

These are common in young children between the ages of four and twelve years. Children complain of deep, relatively diffuse, poorly localised pain in the lower limbs – only at night. The discomfort is often preceded by strenuous exercise the previous day. The pain is not located in a joint and responds to massage and mild analgesics. The physical examination is normal. Laboratory tests are not indicated, but an erythrocyte

sedimentation rate (ESR) might be useful to screen for inflammatory conditions. These children and their parents can be reassured that they will outgrow the problem. Only symptomatic treatment is required.

### Backache

When children complain of backache, there is often a serious underlying problem. The following conditions should be excluded:

- Tuberculosis of the vertebra (Pott's disease)
- Tumour or infiltration of the spinal cord or spinal column, or other space-occupying lesion
- Spondylitis in older boys

A careful clinical and full neurological examination is indicated. After a plain radiograph has been taken, computerised tomography (CT) or magnetic resonance imaging (MRI), especially of the sacro-iliac joints, may be considered.

### Skin rashes

The skin rashes of connective tissue disorders have to be differentiated from eczema and infective rashes. The distribution of the former is frequently typical on the upper eyelids and 'butterfly' area of the face, or over the knuckles.

### Multi-system disease

Dysfunction or abnormality of more than one organ system may occur in connective tissue diseases, but has to be differentiated from multi-system infection (e.g. tuberculosis, HIV infection) and malignancy (e.g. leukaemia).

### Special investigations in the diagnosis of arthritides

The white cell count, platelet count, ESR and C-reactive protein (CRP) are useful screening tests. It is unlikely that these will all be normal in the presence of an inflammatory condition, infection or malignancy. C-reactive protein, ESR and plasma

viscosity are useful to monitor disease activity.

Rheumatoid factor (RF) and antinuclear antibodies (ANA) both have a low sensitivity and specificity in the diagnosis of juvenile idiopathic arthritis, but can be helpful in prognosis and in ruling out other diagnoses.

Arthroscopy and synovial biopsy are useful in the differential diagnosis of persistent arthritides in childhood, because they can rule out conditions such as tuberculosis.

Imaging can be useful in the differential diagnosis and in assessing control of the disease. Plain radiographs are commonly used to document the disease state at the outset of management. Specialists may advise tomography, arthrograms, ultrasound, radioactive imaging, CT scanning and MRI imaging in appropriate circumstances.

### Juvenile idiopathic arthritis (JIA)

Juvenile idiopathic arthritis, referred to as juvenile rheumatoid arthritis (JRA) in North American literature, is one of the more common paediatric chronic disorders. It can be very disabling and disfiguring. Early diagnosis and vigorous treatment are very important.

Juvenile idiopathic arthritis is diagnosed according to the following criteria:

- Other forms of arthritis are excluded.
- The patient is younger than 16 years at diagnosis.
- Arthritis is present in one or more joints.
- The disease has lasted longer than three months.

Juvenile idiopathic arthritis may present with the following onset patterns during the first six months:

- **Systemic:** persistent high, spiking fever and arthritis, hepatosplenomegaly, or pericarditis

- **Pauci-articular:** up to four joints
- **Poly-articular:** five or more joints

### **Pauci-articular onset juvenile idiopathic arthritis**

This is the most common subtype of JIA. The patient is typically a preschool girl with arthritis of the knee, ankle or elbow. Initially, more than four joints are not involved. In most cases the arthritis is mild, but lasts a few years. One-third of patients will develop poly-arthritis that is difficult to control and 20% will develop anterior uveitis at some stage during their disease. Eye disease (iritis, uveitis) is usually asymptomatic, but can lead to severe visual impairment and blindness. The risk of iritis is greatest in young girls and when antinuclear antibodies are present. Iridocyclitis is diagnosed by slit-lamp examination, but an irregular pupil shows a late complication of posterior synechiae, which is visible to the unaided eye.

### **Poly-articular onset juvenile idiopathic arthritis**

About 35% of patients present with poly-articular disease. This has an insidious onset. The typical patient is a preschool girl with a symmetric arthritis affecting the large joints of the knees, wrists, elbows and ankles. The small joints of the hands and feet, the temporomandibular joints and the cervical spine may be involved early on or late in the course of the disease. Rheumatoid factor-positive patients who contract the disease late in childhood or in adolescence may follow the pattern of adult rheumatoid arthritis. All patients with poly-articular disease have a poorer prognosis than those with a pauci-articular onset. Forty per cent will develop bony erosions and a chronic persisting course, despite treatment

### **Systemic onset juvenile idiopathic arthritis**

Less than 10% of patients present with systemic signs and symptoms. Systemic symptoms and signs may precede arthritis by weeks or even

years. Diagnosis is difficult and certain only in retrospect. Striking features present in early childhood. These include a characteristic fever and rash, serositis (pericarditis, pleuritis), hepatosplenomegaly and lymphadenopathy. The so-called quotidian fever rises above 39°C once or twice a day and then falls to normal. This may respond to prednisone 2 mg/kg/day or to indomethacin 2 mg/kg/day, but not to other antipyretics. The classic rash is fleeting and individual lesions do not last more than a few hours. Erythematous macules 2 to 5 mm in size present on the trunk and proximal

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limbs, and sometimes on the face, palms and soles. The rash is occasionally pruritic. It may appear with the fever and be provoked by a hot bath, psychological stress or scratching. About 50% of children with systemic onset JCA will have destructive polyarthritis that responds poorly to treatment.

### **Management of persistent arthritis in children**

The goals of treatment should be discussed and explained to children and their parents. They should include:

- Relief of symptoms
- Maintenance of joint range of motion
- Maintenance of muscle strength
- Rehabilitation

### **Monitoring of progress**

Control of the disease activity and the impact of the disease on the child and family should be monitored regularly. It is helpful to involve all members of the therapeutic team. Children with active inflammation initially need to be seen at least monthly. Children with well-controlled disease and those in remission should be seen three to six monthly. The range of motion of the affected joints, the muscle bulk of the affected limbs and the ability to function at home, at school and socially should be recorded at least annually. All children with persistent arthritis should have a slit-lamp examination by an ophthalmologist at diagnosis and then every six months for the next seven years. Anti-nuclear antibody-positive girls with pauci-articular onset JIA should have slit-lamp examinations every three months.

### **Non-steroidal anti-inflammatory drugs**

Non-steroidal anti-inflammatory drugs (NSAIDs) are the mainstay of therapy for children with inflammatory arthritis. On the basis of effectiveness, cost and convenience, indomethacin is one of the better NSAIDs. Although a liquid preparation is not commercially available in South Africa, this is easily made up by a pharmacist. After starting an NSAID, at least two months should be allowed to monitor the clinical response – unless there are severe adverse effects. If there has been no active arthritis for six months and the acute phase reactants have been normal, treatment may be stopped. Children tolerate NSAIDs better than adults. The most common adverse effect of NSAIDs is abdominal pain and, to counter this, they should be taken with a meal. If the abdominal pain persists, an antacid is usually effective. Other problems include headache, changes in mood, rashes and, rarely, interstitial nephritis. Headache in children taking indomethacin may respond if therapy is switched to ibuprofen or another NSAID. Care should be taken when

giving NSAIDs to a patient with renal disease, and the combination of methotrexate and NSAIDs should be avoided if renal function is impaired.

### **Cytotoxic agents**

Methotrexate may be added if the arthritis is not adequately controlled by NSAIDs within three months. Begin with 0.3 mg/kg/week, taken as a single dose on an empty stomach. Increase at monthly intervals until there is a satisfactory response or until a maximum of 1 mg/kg/week or 25 mg/week is reached. Folic acid is prescribed for the day following the administration of methotrexate. In cases in which there is a suboptimal response, or where the oral route is not tolerated, intramuscular or subcutaneous injections may be administered at similar or lower doses. Adverse effects include nausea, mood changes, mouth ulcers, raised liver enzymes, bone marrow toxicity, and blood or protein in the urine. Patients should be monitored monthly with history, clinical examination and laboratory tests for liver enzymes (AST, ALT, gamma GT, LDH), full blood count, serum urea and creatinine, and urine blood and protein. Other cytotoxic drugs such as cyclophosphamide or cyclosporin may be also considered. is another, but more expensive and toxic, option.

### **Glucocorticoids**

If at all possible, long-term oral glucocorticoids should be avoided because of their adverse effects. Growth failure and suppression of the hypothalamic-pituitary-adrenal axis are the main concerns. Short-term 'low-dose' prednisone (1 mg/kg/d) may be added to an NSAID and methotrexate when the disease is not adequately controlled or for the systemic phase of systemic onset JCA. Higher doses (2 mg/kg/d) may be used for a week or two to gain control of an acute flare-up, but must then be rapidly withdrawn to the smallest dose possible. So-called pulse therapy, with very high doses given orally (prednisone) or

intravenously (methylprednisolone) over one to three days, is occasionally used for severe exacerbation of JIA. Pulse therapy is potentially dangerous and should only be given if the patient can be closely monitored for clinical status, hypertension and changes in serum glucose and electrolytes.

### **Disease-modifying antirheumatic drugs (DMARD)**

The DMARDs, chloroquine, sulfasalazine, gold, d-penicillamine and colchicines, have a diminishing role in therapy and should be reserved for specialist rheumatologists to prescribe.

### **Intra-articular injection**

Intra-articular injections of long-acting steroids are indicated to alleviate pain and to suppress inflammation in a joint, tendon or bursa that is inflamed out of proportion to other areas, or is not responsive to non-invasive anti-inflammatory therapy. They may also be used to avoid systemic corticosteroids, to avoid an increase in the dosage of systemic steroids, or to decrease the swelling of inflamed soft tissue and relieve nerve entrapment.

### **Physiotherapy and occupational therapy**

Occupational therapy and physiotherapy are essential for severe arthritis. They can provide:

- exercises that increase the range

of movement of joints and increase muscle bulk;

- splinting (e.g. nocturnal resting splints, working splints and dynamic splints), which provides pain relief and prevents contractures;
- shoe inserts to relieve pain from tender heels or sensitive metatarsal heads;
- shoe raises for a short leg to prevent contracture in the longer leg;
- advice on aids for the activities of daily living; and
- specialised assessments to monitor the course of the disease, measure its impact and evaluate the patient's potential for employment.

Children should be encouraged to exercise as much as possible. Teachers should be told about the illness and be given relevant information.

### **Orthopaedic surgery**

An orthopaedic surgeon may be needed to:

- Perform diagnostic arthroscopy and synovial biopsy
- Restore function or relieve pain in severely damaged joints in older children with longstanding disease, by:
  - replacement (arthroplasty)
  - fusion (arthrodesis)
  - realignment (osteotomy)
- Inject or aspirate joints
- Institute traction to relieve pain and restore alignment, particularly for the hip joint

### **Spondylo-arthropathies**

A large group of those children with persistent arthritis fall into the group of spondylo-arthropathies. This group includes juvenile ankylosing spondylitis (JAS), Reiter's syndrome, and the arthritis associated with psoriasis or with inflammatory bowel disease.

Common features of these conditions are:

1. *Seronegativity* – absent rheumatoid factor and antinuclear antibodies.

2. *Enthesitis* – most commonly in the heel pad (insertion of plantar fascia into calcaneus), back of heel (insertion of tendo Achilles into calcaneus), ball of foot (plantar surface of metatarsal heads), bases of first and fifth metatarsals, and tibial tuberosity.
3. *Arthralgia or arthritis*.
4. *Insidious onset of disease* – which may lead to diagnosis being delayed for years.
5. *Ankylosing spondylitis*, which often develops late in the course of the disease.
6. *Family members* with ‘bad backs’, arthritis, ankylosing spondylitis, psoriasis, or inflammatory bowel disease.
7. *Extra-articular manifestations*, including acute iritis.
8. *HLA B27 positive*.
9. *More common in boys* than in girls (except for psoriasis-associated arthritis, which is slightly more common in girls).

**Figure 6:** Enthesitis-related arthritis (juvenile ankylosing spondylitis)



**The SEA syndrome** is defined as the presence of the first three features in a child under the age of 17 years. It overlaps the spondylo-arthropathies and this is where its utility lies: it may predict the future development of one

of the spondylo-arthropathies, especially juvenile ankylosing spondylitis.

### Clinical problems posed by chronic conditions

In caring for a patient with a chronic disorder, the problems faced by the practitioner fall into three categories: the ‘new’ patient, the ‘known’ patient who needs routine care, and the ‘known’ patient who has a severe flare-up of disease. The different demands imposed on the health care team by these three situations are the following:

#### 1. New patient

- Making the diagnosis
- Breaking the news
- Controlling the disease

#### 2. ‘Known’ patients – routine visit

##### Assess disease activity

The history, examination and, where appropriate, special tests should assess the current activity of the disease and answer the question, ‘Is the disease adequately controlled?’

##### Assess disease impact

A chronic disease has an impact on the activities of the patient’s daily life, such as school attendance, participation in social events, writing, dressing, feeding and washing. The social and financial impact on the family (parents and siblings) should also be assessed.

The impact of the treatment should be assessed in terms of the side effects of medication, and in terms of compliance with appointments and therapy.

#### Manage disease and monitor progression and drug side effects

Treatment should be adjusted or maintained according to the control of disease activity and the impact of the disease.

#### Support patient and family, and school teacher

The patient and family need constant support and the school teacher needs to be brought into the health care team. Provide literature and sources of

information and support from organisations such as the Arthritis Foundation.

#### Be aware of ‘alternative’ medicine

The more chronic and severe the disease is, the more certain it is that the patient or parents will want to try ‘alternative’ or ‘complementary’ medicine. This should be discussed with them at the earliest opportunity, and regularly at follow-up visits. Acupuncture is finding a place in orthodox medicine in the treatment of chronic pain and patients may be referred for this. Other modalities, such as diets, copper bracelets and homeopathy, have not been tested in clinical trials and have not been found to have any useful effect.

#### 3. ‘Known’ patient with a chronic disorder who has ‘new’ signs and symptoms

The ‘known’ patient who has an acute exacerbation of the disease, or new signs and symptoms, poses a different set of issues. It has to be decided if this is a flare-up of the disease, a complication of the treatment, or a new and unrelated disease. Such cases demand continued vigilance and care in taking the history and in clinical examination.

#### Final comment

Ongoing care for the chronically ill patient must be provided by the same team of health care workers. The package of care should always be accessible and, as described above, as comprehensive as possible. 🙌

**See CPD Questionnaire, page 34**

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