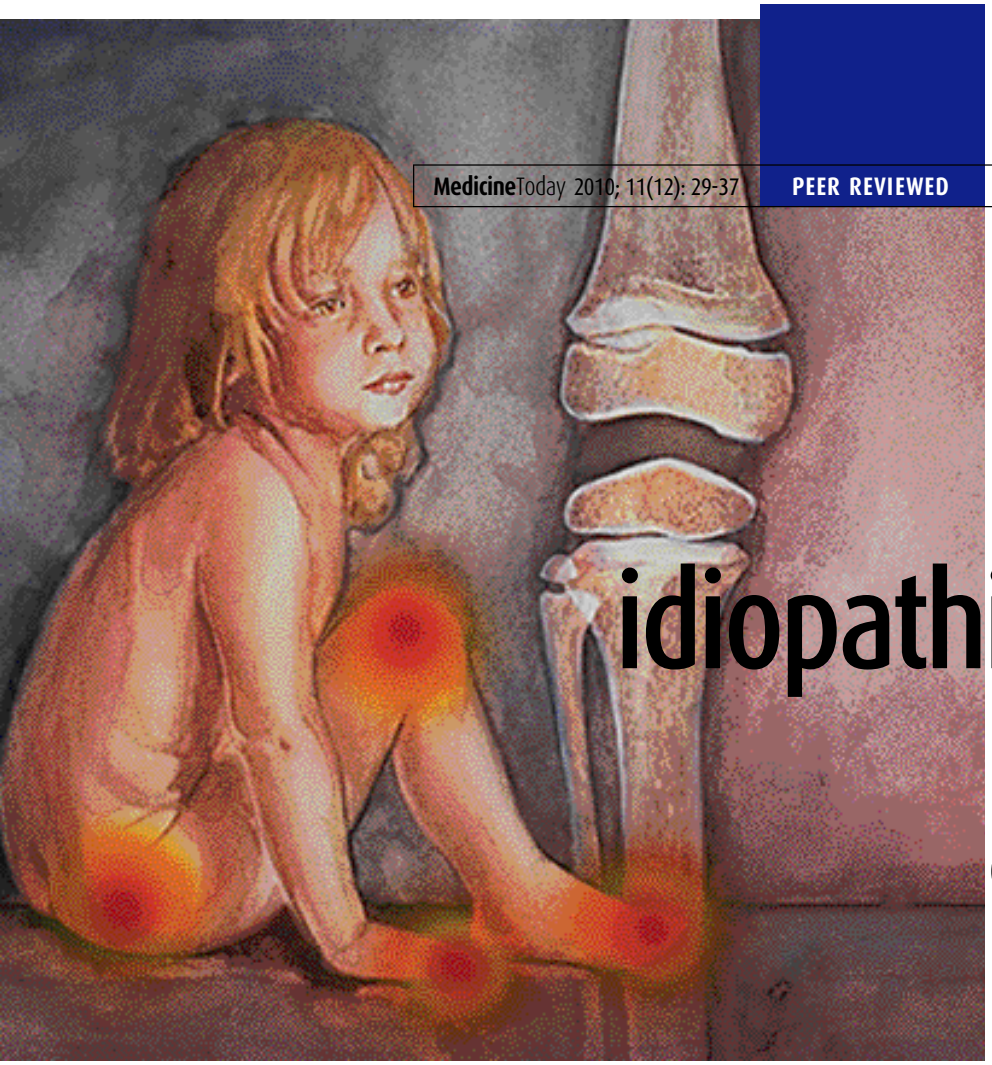
MedicineToday 2010; 11(12): 29-37 PEER REVIEWED POINTS: 2 CPD/2 PDP



Juvenile idiopathic arthritis

an update on diagnosis and management

This article is a summary of the new guidelines on juvenile idiopathic arthritis developed by a specialist advisory group in conjunction with the Royal Australian College of General Practitioners. These guidelines provide recommendations for the early diagnosis and multidisciplinary management of this condition in the primary care setting.

The Royal Australian College of General Practitioners (RACGP) has developed national musculoskeletal clinical guidelines on osteoarthritis, rheumatoid arthritis, juvenile idiopathic arthritis (JIA)[1] and osteoporosis for GPs and other primary care health professionals. These four clinical guidelines have been developed to the requirements of the National Health and Medical Research Council.

Each guideline, has been developed by working groups, including GPs, rheumatologists, consumers and allied health professionals. With funding from the Australian Government

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IN SUMMARY

- **Juvenile idiopathic arthritis (JIA) is a chronic, autoimmune, inflammatory joint disease. It is defined as persistent arthritis of unknown aetiology that begins before 16 years of age and persists for at least six weeks.**
- **JIA occurs in one to four per thousand children in Australia and is the most common rheumatic disease in children and adolescents.**
- **The diagnosis is largely clinical and involves persistently swollen stiff joints.**
- **The aim of treatment is the induction of remission and control of the disease to minimise pain and functional loss, and maximise quality of life. There is currently no cure for JIA, although with the increasingly effective new therapies, long-term disease remission is a realistic aim. A multidisciplinary approach provides optimal treatment.**
- **The prognosis is worsened by late/misdiagnosis and delay in effective therapy.**

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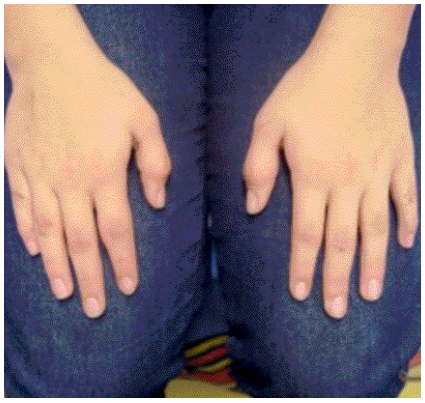

Figure 1. Polyarticular JIA. Note the swelling of the thumb and index interphalangeal joint.

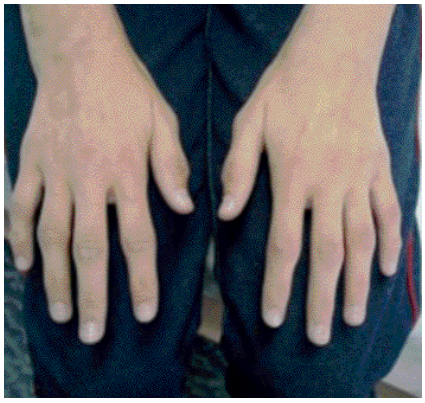

Figure 2. JIA polyarticular symmetric swelling of small joints.

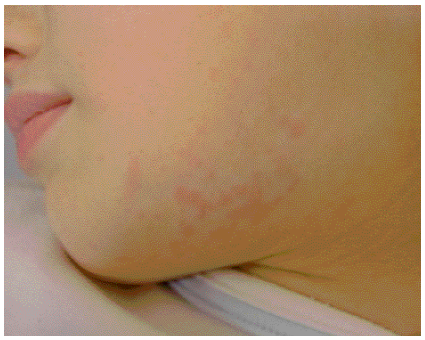

Figure 3. JIA systemic rash (Still's disease).

Department of Health and Ageing, project officers and expert working group members identified and reviewed the best evidence for primary care and compiled the strength of the body of evidence for the Australian guidelines.

At least 5000 children are affected by JIA at any one time in Australia.[2,3] Its prevalence in Australia is estimated to be between one and four cases per 1000 children.[4]

JIA can have significant associated morbidity and mortality. Long-term, follow-up studies have revealed that JIA carries the potential for longer-term inflammatory activity and complications, leaving a lasting impact on patient function, growth and quality of life. Accurate and early diagnosis along with appropriate management and referral are essential for maximising patient outcomes and quality of life. General practice plays an important role within the Australian healthcare system in prevention, early detection and chronic disease management of this condition.

This article, which is mainly a summary of the recent published guidelines on JIA, reflects the current evidence-based approach to managing children with JIA.

Definition and aetiology

JIA is a chronic, autoimmune, inflammatory joint disease and the most common rheumatic disease in children and adolescents. It is defined as persistent arthritis of unknown aetiology that begins before 16 years of age and persists for at least six weeks; it is diagnosed as 'idiopathic' after excluding other known causes of arthritis.

The cause of JIA is unknown, but it is suspected that environmental factors such as viral infections may trigger the condition in genetically susceptible children. However, it is unusual for more than one child in a family to have arthritis.

Classification

There are seven subtypes of JIA, which are outlined below.

- **Oligoarticular.** This affects four or fewer joints and is the most common subtype.
- **Polyarticular** (rheumatoid factor [RhF] negative). This occurs when five or more joints are affected and RhF antibody is not found on blood testing (Figure 1).
- **Polyarticular** (RhF positive). This occurs when five or more joints are affected and RhF is found on blood testing (Figure 2). This subtype may manifest similarly to rheumatoid arthritis in adults.
- **Systemic.** This is arthritis associated with systemic features, including high-spiking fever, evanescent erythematous rash, lymphadenopathy and hepatosplenomegaly (systemic features may precede the arthritis). This bears the eponym 'Still's disease' (Figure 3).
- **Enthesitis related** (previously known as juvenile spondyloarthropathy). This is a chronic arthritis associated with enthesitis (inflammation at insertion of tendons [Figure 4]), ligaments or fascia to bone), or with lower axial skeletal involvement. Human leukocyte antigen (HLA) B27 is present or there is a family history of a first-degree relative with a HLA B27-related disease. A significant proportion of patients will develop sacroiliitis as adults, but back and sacroiliac joint involvement is uncommon during childhood.
- **Psoriatic.** This is a chronic arthritis, usually with asymmetrical involvement of small and large joints, and either the development of psoriasis or other evidence of a psoriatic diathesis – for example, family history in a first-degree relative, nail pits or onycholysis, or dactylitis.
- **Undifferentiated.**

Aim of the guidelines

The guidelines for JIA seek to provide recommendations for the early diagnosis and multidisciplinary management of the condition in the primary care setting. The recommendations focus on the

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primary care practitioner's role in:

- early identification of JIA
- early referral to a paediatric rheumatologist
- prevention of complications associated with JIA
- alleviation/minimisation of pain
- optimal management of acute exacerbations of JIA
- prevention and minimisation of joint damage
- maximisation of function
- optimisation of normal growth and development
- improved quality of life.

Recommendations from the guidelines were developed to optimise treatment of JIA in the general practice setting. Some of these recommendations are outlined below.

Early diagnosis

GPs should aim to diagnose JIA as early as possible to optimise outcomes for patients.

Early referral

Referral of patients to a paediatric rheumatologist is advised for those with confirmed or suspected JIA whose symptoms persist beyond four weeks. Early referral of patients enables aggressive intervention with disease-modifying antirheumatic drugs, which reduce long-term joint damage and disability.

Clinical examination

GPs should base a diagnosis of JIA (and differential diagnoses) on the patient's history and clinical examination in the first instance, with a strong suspicion of JIA indicated by:

- pain and swelling of single or multiple joints
- loss of function
- fever of at least 10 days with an unknown cause, often associated with a transient erythematous rash (in the systemic onset subtype)
- decreased range of motion.

Diagnostic investigations

In the early assessment of patients presenting with painful and swollen joint(s), GPs should support clinical examination with appropriate tests to assist in increasing diagnostic certainty, excluding differential diagnoses and predicting patients likely to progress to erosive disease. Baseline investigations usually include erythrocyte sedimentation rate or C-reactive protein and a full blood count. RhF, anti-cyclic citrullinated peptide (CCP), antinuclear antigen and HLA B27 antigen tests, and plain x-rays should also be considered.

Multidisciplinary care

GPs should encourage and support a management approach based on individual patient needs and involving a multidisciplinary team of health professionals.

Patient information

GPs should provide ongoing, tailored information to support their patients' understanding of the disease, treatment options, possible outcomes and role in management.

Traditional NSAIDs

GPs should prescribe NSAIDs as the initial drug of choice for reducing inflammation and associated pain in patients with JIA. They should not prescribe topical NSAIDs to treat JIA.

Nutritional therapy

GPs should ascertain the calcium intake of children with JIA, and provide advice on increasing daily calcium intake; this usually equates to approximately three dairy servings in primary school aged children. GPs could consider treating some patients with JIA, particularly in those taking concomitant corticosteroid treatment, with oral calcium and vitamin D supplementation.

Exercise

GPs should encourage patients to engage in regular physical activity compatible with their general abilities and restrictions of their disease.

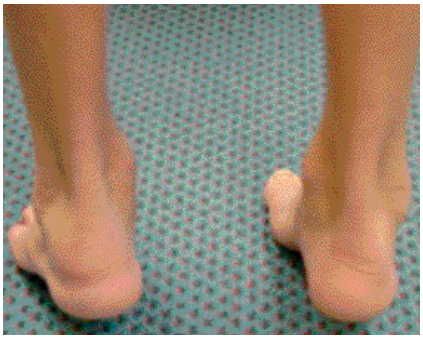

Figure 4. Enthesitis-related arthritis in a boy with HLA B27 present. Note the significant swelling of the left tendo Achilles insertion.

Splints

GPs can inform patients about the use of splints and make individualised recommendations in conjunction with appropriately trained multidisciplinary health professionals.

Foot orthoses

GPs can inform patients with JIA in the lower limb about the role of comfortable, supportive shoes. They could also inform patients about the use of foot orthotics based on an individualised assessment, safety and personal preference, in conjunction with appropriately trained multidisciplinary health professionals.

Complementary/alternative physical therapies

GPs can inform patients and their families who seek advice that there is no validated research to support the benefit of complementary/alternative physical therapies in children with JIA.

Disease monitoring

GPs should be involved in monitoring disease progression and managing comorbidities in conjunction with the treating paediatric rheumatologist.

The diagnosis of JIA should be based

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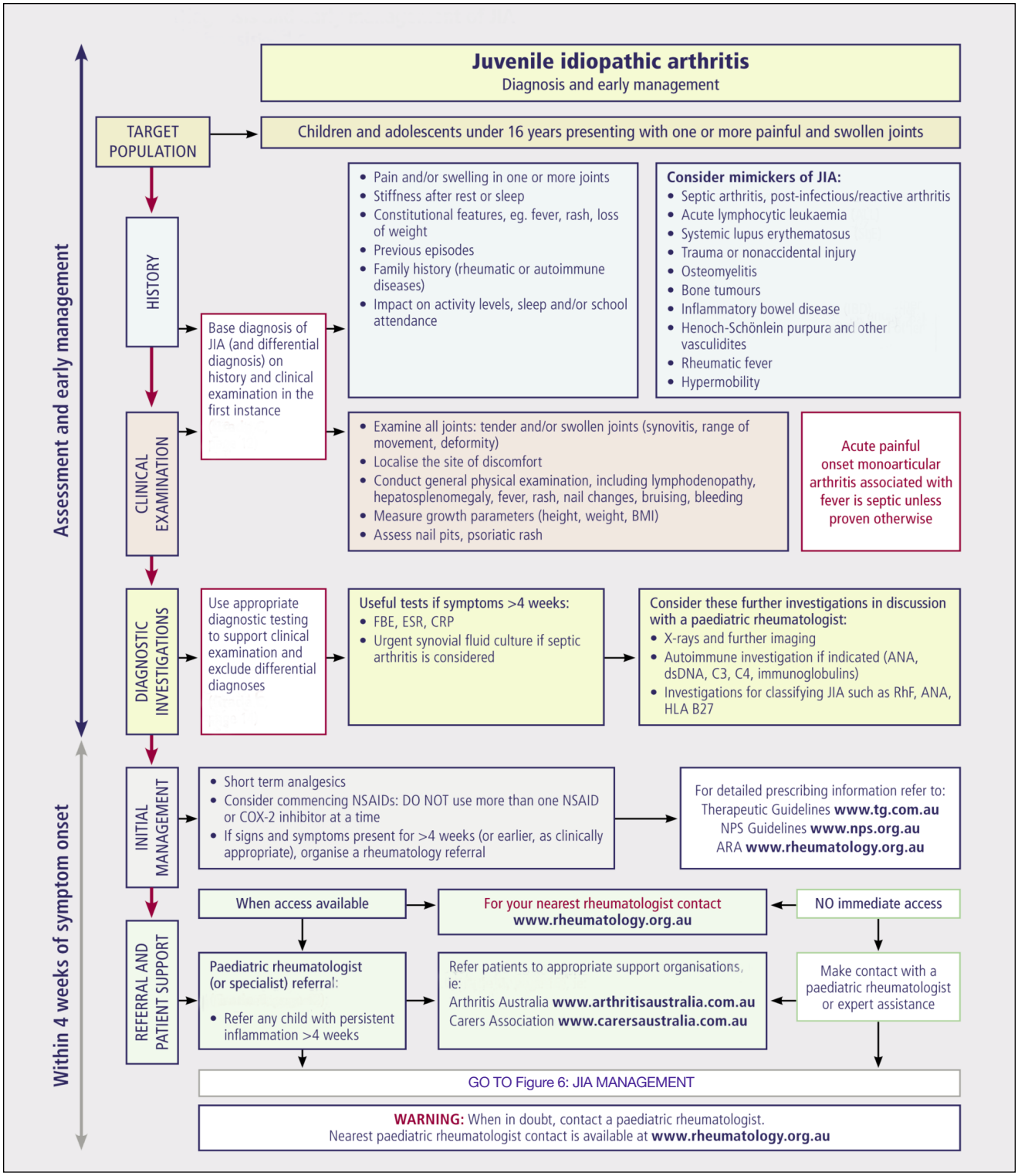

Figure 5. Diagnosis and early management of JIA.*[1]

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ABBREVIATIONS: ANA = antinuclear antigen; CRP = C-reactive protein; COX-1 = cyclo-oxygenase-1; dsDNA = double stranded DNA; ESR = erythrocyte sedimentation rate; FBE = full blood examination; HLA B27 = human leukocyte antigen B27; JIA = juvenile idiopathic arthritis; RhF = rheumatoid factor.

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primarily on careful history taking and clinical examination. Patients commonly present with pain and stiffness in one or more joints. JIA should be particularly suspected in patients who present with persistent joint pain and swelling. In most patients, symptoms emerge over weeks to months.

History

The presenting symptom and sign of JIA almost always involves pain or swelling in one or more joints. It is often of a rather insidious nature and commonly (mistakenly) attributed to minor trauma.

It is important to differentiate acute onset monoarticular arthritis associated with fever, which must be presumed septic until proven otherwise.

A very important and consistent clinical feature is the timing of symptoms during the day. As a general guide:

- early morning stiffness and/or stiffness after rest or sleep suggests an inflammatory cause
- postactivity pain suggests a mechanical cause.

When taking a history it is important to check if there are any concurrent infections (respiratory, enteric or skin). viral infections are probably the most common trigger of transient arthritis.

The definition of JIA includes a chronic duration as most postviral and reactive arthritis has resolved by six weeks. In the systemic onset disease, children with JIA are unwell therefore constitutional features, such as fever, rash and loss of weight, should also be checked. It is also important to find out if the child has been taking any medications (e.g. cefaclor) that may cause an allergic periarticular swelling. The most symptomatic site (joint, muscle, adjacent bone or a more diffuse area) as reported by the child, or parent, should be enquired about.

It is essential to check for extra-articular symptoms by ensuring a thorough systems review and keeping the differential diagnoses of JIA in mind (see Table 1).

It is also important to assess whether normal activity levels or interests have been interrupted and the functional milieu of the patient (e.g. school progress and attendance, sleep pattern, family and peer relationships, and stress experiences). The family history of the patient should also be checked for other types of inflammatory arthritis, particularly the spondyloarthropathies, autoimmune disorders and pain syndromes (e.g. fibromyalgia or other models of pain behaviour).

Examination

The patient should be observed as he or she moves around the room, looking for limitations or alterations in function. It is important to be vigilant when examining these patients. The doctor should:

- examine all joints, not only the site of the presenting complaint. There may be inflammation without symptoms in JIA
- aim to localise the site of maximal discomfort (e.g. is it the joint capsule, adjacent bone or muscle belly)
- examine the patient for signs of systemic diseases with an articular component, extra-articular features of JIA, or both. In particular examine the skin, eyes, abdomen, nails and lymph nodes.

A musculoskeletal assessment should include an examination of:

- joints – look for signs of inflammation such as swelling or tenderness, and assess the range of movement and deformity. Joints affected by JIA are typically swollen, may be somewhat tender to touch and warm but are usually not erythematous
- entheses – bone attachment sites of ligaments/tendons (e.g. Achilles tendon)
- tendon sheaths of fingers and toes (e.g. dactylitis in psoriasis)
- gait – antalgic (pain) or limp, Trendelenburg's sign
- muscle tenderness, muscle wasting or weakness (e.g. inability to toe or crouch walk). Look at the shoe sole and heel-wearing pattern
- leg length measurement
- spinal flexion, including Schober's test (the measurement of the lumbosacral range should increase in distance by at least 6 cm on maximal flexion with knees straight; the starting range is a point 5 cm below and 10 cm above the lumbosacral junction [use the dimples of venus as a guide for this]).

Figure 5, which has been reproduced from the guidelines, details the procedure for diagnosing and managing (in the initial stages) patients with JIA.[1]

Table 1. Differential diagnoses of JIA

Juvenile idiopathic arthritis (JIA) can resemble any disorder causing acute or chronic arthritis in children. Exclusion of other disease diagnoses is therefore a necessary step in the diagnosis of JIA. The following diagnoses should be kept in mind:

- septic arthritis
- postinfectious/reactive arthritis
- systemic lupus erythematosus
- acute lymphoblastic leukaemia
- trauma/nonaccidental injury
- osteomyelitis
- bone tumour
- inflammatory bowel disease
- Henoch-Schönlein purpura and other vasculitides
- rheumatic fever
- hypermobility

Investigation

It may seem self-evident but investigating children with arthritis should occur in those who have clinical evidence of inflammatory disease and not pain alone as the only symptom. There is no single test that can be used to accurately diagnose JIA and many of the tests mentioned below have low sensitivity and specificity

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for JIA. A rheumatologic blood screen is fraught with a high degree of both false-positive and false-negative results.

Elevated erythrocyte sedimentation rate and C-reactive protein level indicate an inflammatory process but have low specificity for JIA. These markers are usually elevated in children with JIA, but may also be normal particularly in less severe disease.

RhF and anti-CCP antibody are not diagnostic of all JIA because they only occur in a select subgroup. RhF is positive in only a small percentage of patients with JIA (usually teenage girls with symmetric polyarthritis). If the anti-CCP test is positive, the level of anti-CCP may indicate the likelihood of aggressive disease progression and a poorer prognosis. A full blood count test is usually undertaken to provide general information relating to inflammation and anaemia.

Antinuclear antibody test is positive in up to 10% of the normal childhood population. It is important to judge this test by the company it keeps – for example, is there definite joint swelling or only arthralgia?

Serial x-rays over years may show disease progression and therefore indicate the need for a change in treatment strategy. MRI and ultrasound are best reserved until the patient has been clinically assessed by the specialist due to the often unnecessary expense.

Treatment

The aim of treatment of children with JIA is the induction of remission and control of the disease to minimise pain and functional loss, and maximise quality of life. There is currently no cure for JIA, although with the increasingly effective new therapies, long-term disease remission is a realistic aim. JIA treatment has altered as a result of recent research into the best practice approach to managing children. Figure 6, which has been reproduced from the guidelines, outlines the procedure for managing children with JIA.

Table 2. Recommended dosages of oral NSAIDs for children with JIA*[1]

Drug	Dosage
Celecoxib	2–4 mg/kg twice daily
Diclofenac	1 mg/kg twice daily
Ibuprofen	10 mg/kg three to four times daily
Indomethacin	0.5–1.0 mg/kg two to three times daily
Meloxicam	0.15–0.30 mg/kg twice daily
Naproxen	5–7.5 mg/kg twice daily
Piroxicam	0.2–0.4 mg/kg once daily

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Traditional NSAIDs

GPs should prescribe NSAIDs as the initial drug of choice for reducing inflammation and associated pain in patients with JIA (Table 2). Recommendations for managing children with JIA with NSAIDs include the following points.[1]

- Prescribe only one NSAID at a time.
- Long-term use of NSAIDs should be at the lowest effective dose.
- NSAIDs may be taken with methotrexate.
- Use NSAIDs in the liquid form for children unable to swallow tablets.
- Base the selection of NSAIDs on dosing requirements, availability and patient preferences (e.g. taste).
- Consider stopping NSAIDs and COX-2 inhibitors seven to 10 days before any major surgical procedure, particularly orthopaedic surgery. Discuss with the surgeon and make a decision on a case-by-case basis.

NSAIDs are generally well tolerated by children, but toxicity can occur. Caution should be applied in view of the known side effects (increased sleep disturbance and nonspecific abdominal pain), although these tend to be less common or severe than in adults.

A pseudoporphyria-like skin reaction occurs in about 5% of children taking naproxen. This complication is more common in fairer skinned children who are living in sun-exposed latitudes. The antiplatelet effect of the NSAIDs predisposes to excessive bruising in particularly active children.

Most children with asthma can take NSAIDs safely. However, those with diagnosed or suspected aspirin-induced asthma (symptoms of asthma usually accompanied by facial flushing and rhinitis within three hours of exposure to an NSAID) should avoid all NSAIDs. Long-term aspirin use is not recommended in children with JIA because of the link with Reye's syndrome.

NSAIDs are the first-line drug for the treatment of inflammation in children with JIA. They have well established analgesic and anti-inflammatory effects; however, they do not influence progression of the disease and do not prevent joint damage. Children usually tolerate NSAIDs very well, with few side effects.

Disease-modifying antirheumatic drugs (DMARDs)

In caring for children with arthritis, the initiation of DMARD medication, and altering of dosages, is seen as the role of the specialist paediatric rheumatologist. A GP has an important role

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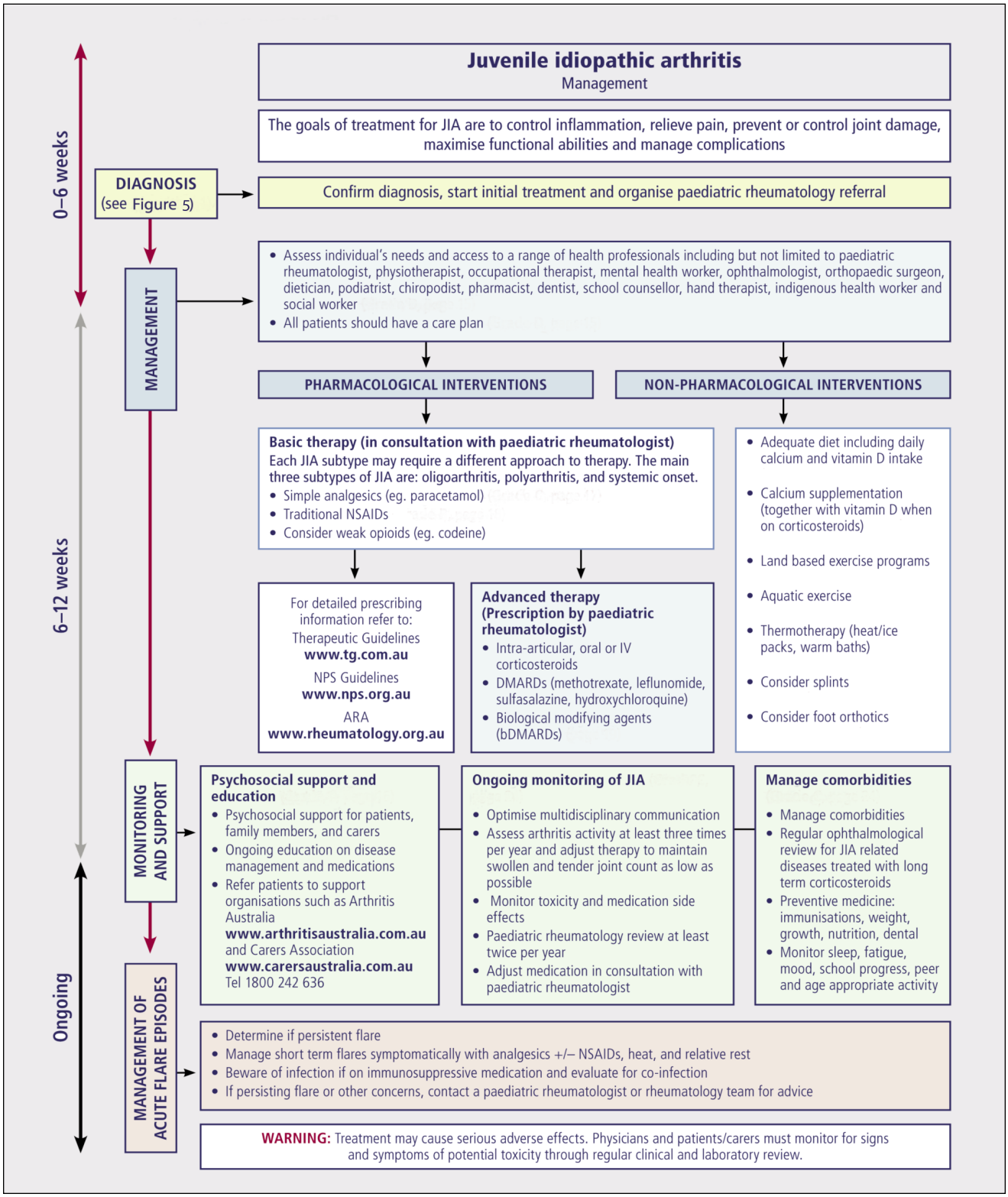

Figure 6. Management of JIA.*[1]

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ABBREVIATIONS: DMARDs = disease-modifying antirheumatic drugs; JIA = juvenile idiopathic arthritis.

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in monitoring children's adherence to DMARDs and their side effects. For example, common side effects of methotrexate treatment include nausea, anticipatory nausea, mouth ulcers and abdominal discomfort, and less commonly, altered liver function (increased transaminases), infection and haematological toxicity.

Other commonly used DMARDs include prednisolone hydroxychloroquine, sulfasalazine, leflunomide and the newer biological DMARDs.

Intra-articular corticosteroids

Corticosteroid injections into the joints using long-acting preparations such as triamcinolone hexacetonide have an extremely important role in the overall management of juvenile arthritis and are very effective in suppressing inflammation and maintaining function. In most children, administration of this medication requires sedation or anaesthesia.

Nutritional therapies and calcium supplementation

Appropriate caloric and calcium intake should be encouraged. Children with JIA taking corticosteroid therapy are at increased risk of osteoporosis and osteopenia. Additional consideration should be given to calcium and vitamin D supplements when children are taking a course of corticosteroids.

Monitoring disease progression and managing comorbidities

Recommendations for monitoring disease progression and managing comorbidities include the following points.

- Paediatric rheumatology review should take place regularly and be adjusted according to disease severity.
- Regular screening for uveitis is recommended.
- Arthritis activity should be assessed at least three times per year and treatment should be adjusted to keep the swollen and tender joint count as low as possible.
- Patients need to be monitored for potential toxicity and side effects of medications.
- Frequency and type of monitoring will depend on the DMARD prescribed, but most patients will require a full blood count (to monitor for marrow suppression) and liver function tests (to look for raised transaminases as a sign of hepatotoxicity) approximately monthly to three monthly (once on a stable dose).

Prognosis

For many years it was believed that most children eventually outgrow JIA. It is now known that half of all children with JIA will still have active arthritis 10 years after diagnosis unless treated appropriately. In moderate to severe cases, JIA can produce serious joint and tissue damage and cause problems with bone development and growth. In some cases, JIA symptoms are mild and do not cause progressive joint disease and deformities.

In the past, JIA has often been viewed as a benign condition, which it is not. Children presenting with JIA may be diagnosed inappropriately as having nonspecific joint pains, 'growing pains' or recurrent musculoskeletal 'sprains'. As a result appropriate referral of the patient and treatment are delayed.

The outcomes for children with JIA are improved if they are managed by a multidisciplinary team with the input of a paediatric rheumatologist.

Conclusion

This article reviews the management of JIA according to the recently published RACGP guidelines on this condition. Early recognition of the signs and symptoms of JIA will help improve the prognosis of affected children and adolescents. MT

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Further reading

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COMPETING INTERESTS: Dr Chaitow has been on the advisory board to Wyeth Pharmaceuticals.

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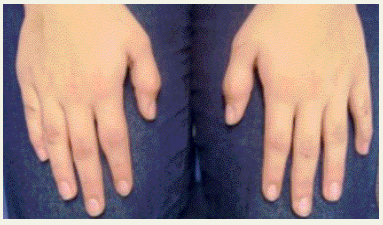

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