# Outcomes for Juvenile idiopathic arthritis

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## Abstract

Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatological disease of childhood. Despite the current availability of potent disease modifying anti-rheumatic medications, most children still experience a chronic course with prolonged periods of active disease. Goals for treatment should include disease remission with optimal physical functioning allowing children to lead normal lives without structural joint damage. However, recent studies demonstrate only moderate rates of achievement of remission, indicating that JIA is not as benign as previously thought, with approximately 50% of adults suffering from persistent inflammation and disability. There is a shift towards early aggressive treatment to limit inflammation and achieve a normal lifestyle, since there is some evidence for a better long term prognosis with this approach. The development of drugs such as the anticytokine agents for disease resistant to conventional treatment has improved disease management and renders historical cohorts of patient outcomes rapidly outdated. This review briefly describes the condition, and current and longer term data on outcomes for this common chronic childhood condition.


**Keywords** arthritis; child; Juvenile idiopathic arthritis; outcome/s

## Definition and classification

JIA is defined as arthritis (swelling or limitation of motion of the joint accompanied by heat, pain or tenderness) of unknown aetiology beginning before the 16th birthday and persisting for at least six weeks where other known conditions are excluded. Historically there have been a number of classifications, but that of the International League of Associations for Rheumatology (ILAR) is now the most widely accepted (published in 2004). This is important primarily for research purposes, but is also a useful clinical tool in discussing prognosis with children and families. See Table 1 for the ILAR classification of JIA.

## Epidemiology and aetiology

Determining incidence and prevalence is challenging because of differing classifications and inclusion criteria. In the UK, JIA has an approximate incidence of 1 in 10,000 and a prevalence of 1 in 1000 with a female predominance. The aetiology remains unknown. There is some enthusiasm for the hypothesis of an autoimmune process with an environmental trigger in a genetically susceptible host. Twin and sibling studies lend weight to this theory. In order to exclude other conditions, the clinician must consider the differential diagnosis, listed in Table 2.

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### Pathophysiology

There is good evidence that T-cells play an important role, with recruitment to the joint by up-regulation of adhesion molecules on synovial endothelium, and retention in the joint of activated cells. Pro-inflammatory cytokine levels in the joint are high, released from T-cells (TNF-$\alpha$, Inf-$\gamma$, IL2, MIF) and from monocytes (TNF, IL1, IL6, IL8, IL12). Regulatory T-cells and anti-inflammatory cytokines (IL4, IL10 and TGF $\beta$) appear reduced. A number of HLA class I and class II antigens are found in association with subtypes of JIA. For example HLA-A2 is associated with early onset oligoarthritis in girls.

## Clinical features

### Pointers in the history

Key features to elicit are the nature, severity and duration of morning stiffness and pain, and 'gelling' (the same symptoms) after sitting still for a time. In inflammatory arthritis, swelling of a joint lasts for at least two weeks. The child or young person's functioning at home and at school is critical to the assessment. What can they do for themselves? What do they need help with that they used to be able to do?

### Pointers in the examination

'Every joint, every time' Since children may not be able to express where there is pain and stiffness it is critical that every joint is examined on every contact with the clinician. All too often a child with a swollen knee is subjected to a knee aspiration for presumed sepsis, when further careful examination would have also revealed a toe dactylitis or a swollen, hot, restricted ankle. It is particularly helpful in all ages to examine the ankle from behind whilst the child is standing, looking for any loss of definition of the Achilles tendon. Perform a PGALS (paediatric gait, arms, legs, spine) for screening and hone in on affected joints for detailed examination (DVD available from ARUK, or arthritisresearchuk.org).

Perform a careful systematic examination at the initial assessment (rash, nail changes, mouth ulcers, hepato-splenomegally, respiratory or cardiac findings, weakness, scalp/hair changes etc).

### Investigations

No investigation is diagnostic of JIA. The diagnosis is made clinically with consistent investigation findings on haematological testing (although these may all be normal) and imaging (see Table 2).

## Management

Children with JIA should be assessed by a paediatric rheumatologist and managed within a multi-disciplinary team of experienced and properly trained professionals, that includes a nurse specialist, physiotherapist, occupational therapist, ophthalmologist, play specialist, psychologist, orthopaedic and musculoskeletal radiology consultants, orthotist, and dietician (see standards of care guidelines from Arthritis and Rheumatism Musculoskeletal Alliance/British Society for Paediatric and Adolescent Rheumatology (ARMA/BSPAR)).

## The ILAR classification of JIA

**Systemic arthritis**

Arthritis with or proceeded by daily fever of at least two weeks duration that is documented to be quotidian* for at least three days, and accompanied by one or more of the following:

- Evanescent, non-fixed, erythematous rash
- Generalized lymph node enlargement
- Hepatomegaly and/or splenomegaly
- Serositis**

Exclusions: a–d (see below)

*Quotidian fever is defined as a fever that rises to >39 °C once a day and returns to<37 °C between fever peaks

**Pericarditis and/or pleuritis and/or peritonitis

**Oligoarthritis**

Arthritis affecting one to four joints during the first six months of disease. Two subcategories are recognized:

- Persistent oligoarthritis – affects no more than four joints throughout the disease course
- Extended oligoarthritis – affects a total of more than four joints after the first six months of disease

Exclusions: a–e (see below)

**Polyarthritis (RF negative)**

Arthritis affecting five or more joints during the first six months of disease; tests for RF are negative

Exclusions: a–e (see below)

**Polyarthritis (RF positive)**

Arthritis affecting five or more joints during the first six months of disease; two or more tests for RF at least three months apart are positive

Exclusions: a–e (see below)

**Psoriatic arthritis**

Arthritis and psoriasis or arthritis and at least two of the following:

- Dactylitis+
- Nail pitting++or onycholysis
- Psoriasis in a first degree relative

Exclusions: b–e (see below)

+Swelling of one or more digits, usually asymmetrical, extending beyond the joint margin

++A minimum of two pits on any one or more nails at any time

**Enthesitis related arthritis**

Arthritis and enthesitis-, or arthritis or enthesitis with at least two of the following:

- Sacroiliac tenderness and/or inflammatory lumbosacral pain (at rest with morning stiffness, improves on movement)
- The presence of HLA-B27 antigen
- Onset of arthritis in a male over six years of age
- Acute (symptomatic) anterior uveitis
- History of ankylosing spondylitis, enthesitis related arthritis, sacroiliitis with inflammatory bowel disease, Reiter's syndrome or acute anterior uveitis in a first degree relative

Exclusions – a,d,e (see below)

-Tenderness at the insertion of a tendon, ligament, joint capsule or fascia to bone

**Undifferentiated arthritis**

Arthritis that does not fulfill inclusion criteria for any category, or is excluded by fulfilling criteria for more than one category

**Table 1** (*continued*)

**Exclusion criteria**

a Psoriasis or a history of psoriasis in the patient or a first degree relative

b Arthritis in an HLA-B27 positive male beginning after the sixth birthday

c Ankylosing spondylitis, enthesitis related arthritis, sacroiliitis with inflammatory bowel disease, Reiter's syndrome or acute anterior uveitis or a history of one of these disorders in a first degree relative

d The presence of IgM rheumatoid factor on at least two occasions more than three months apart

e The presence of systemic JIA in the patient

**Table 1**

The objective of medical management has changed in recent years with an emphasis on early and aggressive treatment to suppress inflammation and prevent progression to the complications detailed below. Whilst NSAIDS may help with pain, and to a lesser extent inflammation and swelling, they do not lead to remission. To this end intra-articular corticosteroid (Triamcinolone Hexacetonide) is used early with progression to methotrexate as the first line disease modifying anti-inflammatory drug (DMARD). Those with polyarticular and systemic disease frequently require pulses of systemic steroid medication to control symptoms whilst waiting for DMARDs to be effective. If there is failure of control, despite a good dose (at least 15 mg/m$^2$) of methotrexate for at least 3 months, biologic therapy is used, in accordance with NICE guidance.

Consideration must be given very early to transition to adult services by empowering the young person to be seen alone, take control of their care, encouraging self-advocacy skills, addressing teenage issues – all over a number of years and, when appropriate, introducing them to the adult team and moving them into adult care.

## Monitoring of disease activity

At present JIA cannot be cured. It is managed with drugs that suppress the immune system, which may cause significant side effects. For some, long term remission is achieved. It is critical that the effect of the medication on the disease in the particular patient is monitored carefully and adjusted accordingly. There are several validated tools to monitor disease activity and function described here, to allow interpretation of the outcome data that follows.

### 'Acute' disease activity measures

The American College of Rheumatology (ACR) core outcome variables form the standard measurements of disease activity used in most clinical trials in JIA and are commonly recorded in clinic. The 6 variables are:

- Active joint score – those joints with tenderness and/or pain and/or swelling – out of 71 joints
- The restricted joint score – those joints with a limited range of movement and may count joints with previously active disease – out of 71 joints.