Outcomes for juvenile idiopathic arthritis

Kate Armon

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 remission, indicating that JIA is not as benign as previously thought. The probability of attaining remission within 5 years is approximately 50% across all JIA categories except for polyarthritis when the outlook is significantly worse. Longer term, about 50% of adults with JIA suffer from persistent inflammation and disability.

There is a shift towards early aggressive treatment with the intention to switch off inflammation since there may be a 'window of opportunity' before the disease becomes chronic. There is clear evidence for improved outcome in adult patients treated with this approach ('treat to target') but limited paediatric evidence to date. The explosion in anticytokine agents for treatment of disease resistant to conventional therapy has expanded our armamentarium, improving short term clinical outcomes, but it is still unclear whether we have achieved significant improvements in outcome longer term. This review describes the disease and current and longer-term data on outcomes for this common chronic childhood condition.

Keywords arthritis; child; juvenile idiopathic arthritis; outcomes

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. Accurate classification is important primarily for research purposes, but is also a useful clinical tool in tailoring treatment and discussing prognosis with children and families. See Table 1 for the ILAR classification of JIA. In order to exclude other conditions, the clinician must consider the differential diagnosis, listed in Table 2.

Kate Armon ***BMedSci BMBS MRCP FRCPCH DM*** *is Consultant Paediatric Rheumatologist, Addenbrookes Hospital, Cambridge, UK.* *Conflict of interest: delivered teaching for Abbvie pharmaceuticals and received an honorarium which was paid into a hospital charity account. Have received charitable funding from Pfeizer into our charity account to fund paediatric rheumatology adolescent independence break weekends.*

Epidemiology and aetiology

In the UK JIA has an approximate incidence of one in 10,000 and a prevalence of one in 1000 with a female predominance. It is described in all races and geographic areas, but large variations exist – thus incidence reports range from 1.6 to 23 per 100,000 and prevalence 3.8 to 400 per 100,000 in different races and/or geographical areas. The aetiology remains unknown, but is likely to differ by sub-type. There is enthusiasm for the hypothesis of an auto-immune process with an environmental trigger in a genetically susceptible host. The Human Leucocyte Associated (HLA) loci have long been known to be associated including class 1 (HLA A2 and HLA B27) and class 2 (HLA DRB and HLA DP). Genome wide association studies (GWAS) have identified many potential non-HLA loci too.

Pathophysiology

Chronic inflammation with the innate and adaptive immune systems playing a role is key. T-cells appear to 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-α, Inf-γ, IL2, MIF) and from monocytes (TNF, IL1, IL6, IL8, IL12). Regulatory T-cells and anti-inflammatory cytokines (IL4, IL10 and TGF β) appear reduced.

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 revealed a toe dactylitis or a swollen, warm, restricted ankle. Equally a young person may not have noticed (or prefers not to reveal) their knee flaring as it may necessitate more medication.

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 – available from Arthritis Research UK) for screening and hone in on affected joints for detailed examination.

Perform a careful systematic examination at the initial assessment (e.g. document rash, nail changes, mouth ulcers, hepatosplenomegaly, respiratory or cardiac findings, muscle weakness, scalp/hair or eye changes.)

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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:

1. Evanescent, non-fixed, erythematous rash.
2. Generalised lymph node enlargement.
3. Hepatomegaly and/or splenomegaly.
4. 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:

1. Persistent oligoarthritis - affects no more than four joints throughout the disease course.
2. 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:

1. Dactylitis+
2. Nail pitting++or onycholysis
3. 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:

1. Sacroiliac tenderness and/or inflammatory lumbosacral pain (at rest with morning stiffness, improves on movement)
2. The presence of HLA-B27 antigen
3. Onset of arthritis in a male over six years of age
4. Acute (symptomatic) anterior uveitis
5. 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.

Exclusion Criteria

a. Psoriasis or a history of psoriasis in the patient or a first degree relative
b. Arthritis in a HLA-B27 positive male beginning after the sixth birth-day
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

Investigations

No investigation is diagnostic of JIA. The diagnosis is made clinically with consistent investigation findings on blood testing and imaging (see Table 2). All blood tests may be normal in JIA.

Management

Children with JIA should be assessed by a Paediatric Rheumatologist and managed within a multi-disciplinary team (see National Service Specification for JIA and Standards of Care Guidelines from Arthritis and Rheumatism Musculoskeletal

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