Annals of the Rheumatic Diseases

Leaders

Classifying childhood arthritis

The year 1997 marks the 100th anniversary of the publication of Sir George Frederic Still's landmark paper "On a form of chronic joint disease in children".[1] In recognising childhood arthritis as distinct from adult arthritis, Still fired the first shots in the war of words about its nomenclature and classification which continues to this day. It is now well recognised that childhood arthritis covers a heterogeneous group of diseases, many of which (but not all) have important differences from adult arthritides. Unfortunately, the names of the diseases, and their classification criteria, remain problematic. Still warned against the pitfalls of such debates in the preface to the fourth edition of his paediatric textbook; ". . . we must be careful lest we mistake words for things, and think that new nomenclature means new discovery, and that difference of terms is equivalent to distinction of kind".[2]

The aim of this leader is to discuss the classification of childhood arthritis. Over recent times this has been the focus of several papers,[3 4] a couple of lively debates,[5] and many heated private arguments! It has been difficult to reach agreement on the need for a new classification, let alone arrive at a consensus on the classification itself. However, most paediatric rheumatologists now recognise that the disparities between the European designation "JCA" and the North American designation "JRA" need to be resolved to facilitate international communication and research efforts in the aetiology and treatment of chronic arthritis in children. It is my personal view that the latter remains the prime purpose for reclassifying these diseases—to facilitate research by studying homogeneous disease groupings, rather than to provide a system of nomenclature covering every single form of arthritis in children.

The arguments concerning the current systems of classification have been well rehearsed,[3] and will not be discussed extensively here. Instead, consideration will be given to a proposal for the development of classification criteria for idiopathic arthritides of childhood published just over a year ago by the ILAR/WHO task force for classification criteria in paediatric rheumatology.[6] The classification refers to seven diseases characterised by idiopathic arthritis beginning before the 16th birthday (table). It is based on the clinical experience of paediatric rheumatologists from each of the four regional leagues of the International League Against Rheumatism. As such, it represents the first attempt to reach an international consensus on this subject.[7]

The proposed system has several advantages over current classification systems. Firstly, and perhaps most importantly, it attempts to group clinically distinguishable diseases as distinct entities, rather than put them all under an umbrella term. In fact, each of the seven diseases is supposed to be mutually exclusive. Any patient who has clinical features, apart from arthritis, of more than one of the seven diseases is unclassifiable in this system, an example being the child with psoriatic arthritis who has circulating rheumatoid factor. This reflects the fundamental bias of the system towards research rather than everyday clinical use, as undoubtedly many patients will be unclassifiable. Despite its exclusivity, the system has a degree of flexibility not present in current classifications. For each disease, this takes the form of descriptors which allow further refinement of each disease group, including the age of the child at onset of the arthritis, the pattern of the arthritis, its natural history, and associated laboratory tests. Additionally, the disease "extended oligoarthritis" covers an important group of patients in whom the pattern of arthritis changes from an initial oligoarthritis to a polyarthritis in outcome. The system recognises that many extra-articular clinical features are useful for classification; with particular emphasis on enthesitis and psoriasis. Finally, the proposed system specifies that only a six week period of persistent arthritis is required before the diagnosis can be made, eliminating another JCA/JRA discrepancy.

It must be emphasised that the proposed classification is not finalised, validated, universally acclaimed, or ready for clinical use! Even to colleagues not trained in paediatric rheumatology, it has many shortcomings.[8] One of the most difficult problems is that it is based on inherently subjective criteria. It relies on the examiner's observation of clinical features, including the number of joints involved and the presence of extra-articular features such as enthesitis, psoriasis, "systemic" rash, "generalised" lymphadenopathy, organ enlargement, sacroiliac joint "tenderness", and "inflammatory" spinal pain. Considerable interobserver variability in joint counts has been demonstrated, even between very experienced paediatric rheumatologists,[9 10] and it is likely that similar variability in other clinical features could be documented. Unfortunately there are no objective laboratory criteria on which to base the diagnosis of arthritis in childhood. The biological significance of using the 16th birthday to discriminate childhood from adulthood is questionable,[11] as is the use of a seemingly

Table 1 Proposed classification criteria for the idiopathic arthritides of childhood (abbreviated from reference 6)

Disease		*Criteria*	*Descriptors*	*Exclusions*
1. Systemic Arthritis	Definite:	1. Quotidian fever for at least 2 weeks 2. Evanescent, non-fixed erythematous rash 3. Arthritis	1. Onset age 2. Arthritis pattern (i) oligoarthritis (ii) polyarthritis (iii) no persistent arthritis 4. Disease course[a] 5. Positive ANA 6. Positive RF	NOMID[b] Periodic syndromes[c] Drug hypersensitivity
	Probable:	In the absence of arthritis, 1and 2 (above) plus any two of: 1. Generalised lymph node enlargement 2. Hepatomegaly or splenomegaly 3. Serositis		
2. Polyarthritis RF−		Arthritis of ≥5 joints during the first 6 months of disease	1. Onset age 2. Arthritis pattern (i) symmetric (ii) asymmetric 3. Positive ANA 4. Uveitis	Positive RF
3. Polyarthritis RF+		1. Arthritis of ≥5 joints during the first 6 months of disease 2. Positive RF on at least two occasions 3 months apart	1. Onset age 2. Arthritis pattern (i) symmetric (ii) asymmetric 3. Positive ANA	Family psoriasis
4. Oligoarthritis		Arthritis of 1-4 joints during the first 6 months of disease	1. Onset age 2. Arthritis pattern (i) large joints (ii) small joints (iii) both, mainly upper limb (UL) (iv) both, mainly lower limb (LL) 3. Positive ANA 4. Uveitis	Family psoriasis Family spondylo-arthropathy Positive RF
5. Extended oligoarthritis		1. Arthritis of 1-4 joints during the first 6 months of disease 2. Arthritis of ≥5 joints after the first 6 months of disease	1. Onset age 2. (a) arthritis pattern (i) large joints (ii) small joints (iii) both (UL) (iv) both (LL) (b) arthritis symmetry 3. Positive ANA 4. Uveitis	Family psoriasis Positive RF
6. Enthesitis related arthritis		Arthritis and enthesitis or, in the absence of enthesitis, arthritis and at least two of: 1. Sacroiliac joint tenderness 2. Inflammatory spinal pain 3. HLA B27 4. Family history of at least one of (i) anterior uveitis with pain, redness or photophobia, (ii) spondyloarthropathy confirmed by a rheumatologist, (iii) inflammatory bowel disease 5. Anterior uveitis with pain, redness or photophobia	1. Onset age 2. (a) arthritis pattern (i) large joints (ii) small joints (iii) both (UL) (iv) both (LL) (v) both (UL,LL) (vi) axial (b) arthritis symmetry 3. Arthritis course[d] 4. Positive ANA 5. Uveitis	Positive ANA Positive RF IBD arthritis
7. Psoriatic arthritis		Arthritis and psoriasis or, in the absence of psoriasis, arthritis and a family history of psoriasis in parents or siblings and either: 1. Dactylitis in the patient, or 2. Nail abnormalities (pitting or onycholysis) in the patient	As for enthesitis related arthritis	Positive RF

[a] Disease course (may be obscured by treatment) (i) single episode in remission for at least two years, (ii) persistent arthritis but no systemic features for more than six months, (iii) persistent arthritis and persistent systemic arthritis for more than 6 months, (iv) relapsing disease before the 16th birthday, (v) relapsing disease after the 16th birthday, (vi) others
[b] Neonatal onset multisystem inflammatory disease
[c] Including familial Mediterranean fever, hyper-IgD syndrome, FAPA (fever, aphthous ulceration, pharyngitis, adenopathy).
[d] Oligoarthritis or polyarthritis

arbitrary time point (six months after the disease began) at which to apply the classification criteria.[12] There are several inconsistencies in the criteria and their definitions which may promote heterogeneity within the disease groups and are potentially confusing. These include the definitions of symmetry, dactylitis, positive family history of psoriasis and spondyloarthropathy, and positivity for antinuclear antibody and rheumatoid factor.[8 11] On a more fundamental note, it is clear that any arthritic disease for which an aetiology *is* elucidated (and is therefore no longer "idiopathic") will automatically be excluded from this classification, and thus as a long term solution to classification it is going to be self defeating!

The task force recommended that the proposed classification be validated and compared with existing classifications before being used in a clinical setting. At present, the results of the paediatric rheumatology component of the 12th International Histocompatibility Workshop are being analysed to assess whether the proposed criteria result in patient groups of greater genetic homogeneity than are delineated by the existing classifications. It is only by long term follow up studies, however, that the true validity of the classification will become clear.[13] As G F Still wrote ". . . let us be cautious lest we multiply distinctions; then deem that our puny boundaries are things that we perceive, and not that we have made."[2]

Perhaps an accurate classification cannot be formulated without understanding the aetiology and pathogenesis of the chronic childhood arthritides. It is of great concern, however, that we might never understand the mechanisms of these diseases unless we investigate relatively homogeneous disease groups. We must not allow another

100 years to pass before solving the mysteries of childhood arthritis and it is to be hoped that a flexible, biologically relevant classification will assist that process.

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Uniform structured formats for scientific communications—how far should we go?

Clear, efficient communication is a central aim of any scientific report. Clarity, however, can readily be lost when, as authors, we employ our individual literary style, omit detail that we but not the reader take "as read", present information in long sections without subheadings, and expand reports with comment that relates more to the general topic than the specifics of the study. Following peer review a common request to authors from editors is firstly, to include more detail in the methods and results sections, and secondly, to remove extraneous information and extrapolation from the discussion. Peer review and revision, however, do not always result in optimal presentation of information. There is often disparity between what a study should report and what is actually published. In the case of randomised controlled trials (RCT) this presents important problems for inclusion in systematic reviews[1] and the balanced appraisal of knowledge that may determine clinical practice.

The continuing education of investigators is clearly important if we are to maintain high quality research and communication. One—often underestimated—aspect of this is the experience of peer review. Although primarily established to guide selection for publication, peer review serves an important educational role in directing authors to potential problems and caveats of their study and in suggesting ways of improving presentation and discussion. It is for this reason that the *Annals* editorial office always sends appropriately submitted reports to peer review, even if the Editor's initial appraisal is that the report is sufficiently flawed that it would not be accepted even after

Table 1 CONSORT checklist for randomised controlled trials

Heading	*Subheading*	*Descriptor*	*Was it reported?*	*On what page No?*
Title		Identify the study as a randomised trial		
Abstract		Use a structured format		
Introduction		State prospectively defined hypothesis, clinical objectives, and planned subgroup or covariate analyses		
Methods	Protocol	Describe Planned study population, together with inclusion/exclusion criteria Planned interventions and their timing Primary and secondary outcome measure(s) and the minimum important differences(s), and indicate how the target sample size was projected Rationale and methods for statistical analyses, detailing main comparative analyses and whether they were completed on an intention-to-treat basis Prospectively defined stopping rules (if warranted)		
	Assignment	Describe Unit of randomisation (eg, individual, cluster, geographic) Method used to generate the allocation schedule Method of allocation concealment and timing of assignment Method to separate the generator from the executor of assignment		
	Masking (blinding)	Describe mechanism (eg, capsules, tablets); similarity of treatment characteristics (eg, appearance, taste); allocation schedule control (location of code during trial and when broken); and evidence for successful blinding among participants, person doing intervention, outsome assessors, and data analysts.		
Results	Participant flow and follow up	Provide a trial profile (figure) summarising participant flow, numbers, and timing of randomisationassignment, interventions, and measurements for each randomised group		
	Analysis	State estimated effect of intervention on primary and secondary outcome measures, including a point estimate and measure of precision (confidence interval) State results in absolute numbers when feasible (eg, 10/20, not 50%) Present summary data and appropriate descriptive and inferential statisitics in sufficient detail to permit alternative analyses and replication Describe prognostic variables by treatment group and any attempt to adjust for them Describe protocol deviations from the study as planned, together with the reasons		
Comment		State specific interpretation of study findings, including sources of bias and imprecision (internal validity) and discussion of external validity, including appropriate quantitative measures when possible State general interpretation of the data in light of the totality of the available evidence		