International League of Associations for Rheumatology Classification of Juvenile Idiopathic Arthritis: Second Revision, Edmonton, 2001

The primary aim of the International League of Associations for Rheumatology (ILAR) proposals for classification of juvenile idiopathic arthritis (JIA) is to delineate, for research purposes, relatively homogeneous, mutually exclusive categories of idiopathic childhood arthritis based on predominant clinical and laboratory features. As part of a continuing review process, the ILAR Taskforce on Classification of Childhood Arthritis met in Edmonton in 2001 to discuss modifications to the proposed JIA classification. Since the publication of the first revision of the original classification[1], a number of descriptive studies using the new classification have been reported[2-11]. The aims of this communication are 2-fold: to outline modifications to the revised classification proposed as a result of the Edmonton meeting, and to correct misconceptions highlighted by the published studies concerning the clinical use of the classification.

The Edmonton Revision

The changes embodied in the second revision of the classification are as follows:

1. Clarification of the definitions of each category.
2. Improvement in the congruity between inclusion and exclusion criteria.
3. Removal of the requirement that a dermatologist make the diagnosis of psoriasis.
4. Removal of the requirement that there be medical confirmation of HLA-B27 associated disease in a relative.
5. Reduction in the age for criterion "3" of enthesitis related arthritis, and exclusion "b" from 8 years to 6 years of age.
6. Improvement in the consistency of the structure.

The impracticality of the requirement that a diagnosis of psoriasis be made by a dermatologist was recognized, and this requirement was modified so that the diagnosis of psoriasis could be made by a physician (not necessarily a dermatologist). Similarly, it is no longer required that there be medical confirmation of an HLA-B27 associated disease in a relative as contained in exclusion "c." It is evident that it is very difficult to obtain a reliable history of psoriasis or an HLA-B27 associated disease in a second-degree relative. Therefore, a history of importance to the application of the criteria is restricted to the patient or a first-degree relative (parents or siblings) only. The study of Murray, *et al*[8] indicated that the HLA-B27 association is important in boys over the age of 6 years at onset of arthritis, and this age was substituted for 8 years in exclusion "b." Discrepancies between inclusion and exclusion criteria were resolved, and the exclusions were identified by the letters a, b, c, d, and e. Minor modifications in the definitions in the glossary have been made. It is hoped that these modifications will make the classification more transparent, consistent, and easy to apply. The descriptors suggested in the previous revision are unchanged. They do not form part of the classification as such, but many, such as the presence of antinuclear antibodies (ANA), may be important indicators of outcome, and are worthy of evaluation as possible modifiers of the current classification.

General Definition of JIA

Juvenile idiopathic arthritis is arthritis of unknown etiology that begins before the 16th birthday and persists for at least 6 weeks; other known conditions are excluded.

Exclusions

The principle of this classification is that all categories of JIA are mutually exclusive. This principle is reflected in the list of possible exclusions for each category:

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

b. Arthritis in an HLA-B27 positive male beginning after the 6th 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 2 occasions at least 3 months apart.

e. The presence of systemic JIA in the patient.

The application of exclusions is indicated under each category, and may change as new data become available.

Categories

Systemic Arthritis

Definition: Arthritis in one or more joints with or preceded by fever of at least 2 weeks' duration that is documented to be daily ("quotidian") for at least 3 days, and accompanied by one or more of the following:

1. Evanescent (nonfixed) erythematous rash
2. Generalized lymph node enlargement
3. Hepatomegaly and/or splenomegaly
4. Serositis

Exclusions: a, b, c, d.

Oligoarthritis

Definition: Arthritis affecting one to 4 joints during the first 6 months of disease. Two subcategories are recognized:

1. Persistent oligoarthritis: Affecting not more than 4 joints throughout the disease course

2. Extended oligoarthritis: Affecting a total of more than 4 joints after the first 6 months of disease

Exclusions: a, b, c, d, e.

Polyarthritis (Rheumatoid Factor Negative)

Definition: Arthritis affecting 5 or more joints during the first 6 months of disease; a test for RF is negative.

Exclusions: a, b, c, d, e.

Polyarthritis (Rheumatoid Factor Positive)

Definition: Arthritis affecting 5 or more joints during the first 6 months of disease; 2 or more tests for RF at least 3 months apart during the first 6 months of disease are positive.

Exclusions: a, b, c, e.

Psoriatic Arthritis

Definition: Arthritis and psoriasis, or arthritis and at least 2 of the following:

1. Dactylitis
2. Nail pitting or onycholysis
3. Psoriasis in a first-degree relative

Exclusions: b, c, d, e.

Enthesitis Related Arthritis

Definition: Arthritis and enthesitis, or arthritis or enthesitis with at least 2 of the following:

1. The presence of or a history of sacroiliac joint tenderness and/or inflammatory lumbosacral pain
2. The presence of HLA-B27 antigen
3. Onset of arthritis in a male over 6 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.

Undifferentiated Arthritis

Definition: Arthritis that fulfills criteria in no category or in 2 or more of the above categories.

Descriptors

A number of "descriptors" have been proposed to gather further information on the patterns of the clinical picture. These include age at onset, further description of the arthritis (large joints, small joints, symmetry, upper or lower limb predominance, and individual joint involvement), disease course (number of joints), presence of ANA, chronic or acute anterior uveitis, and the HLA allelic associations. The potential value of ANA as a diagnostic criterion has received a great deal of attention, but there is insufficient evidence to support its inclusion at this time. The descriptors are not part of the classification of JIA, but new data about them may allow reclassification in the future.

Definitions of Terms

Arthritis: Swelling within a joint, or limitation in the range of joint movement with joint pain or tenderness, which persists for at least 6 weeks, is observed by a physician, and is not due to primarily mechanical disorders or to other identifiable causes.

Dactylitis: Swelling of one or more digits, usually in an asymmetric distribution, which extends beyond the joint margin.

Enthesitis: Tenderness at the insertion of a tendon, ligament, joint capsule, or fascia to bone.

Inflammatory lumbosacral pain: Lumbosacral spinal pain at rest with morning stiffness that improves on movement.

Nail pitting: A minimum of 2 pits on one or more nails at any time.

Number of affected joints: Joints that can be individually evaluated clinically are counted as separate joints.

Positive test for rheumatoid factor (RF): At least 2 positive results (as routinely defined in an accredited laboratory), at least 3 months apart, during the first 6 months of disease.

Psoriasis: As diagnosed by a physician (but not necessarily a dermatologist).

Quotidian fever: Fever that rises to ≥ 39°C once a day and returns to ≤ 37°C between fever peaks.

Serositis: Pericarditis and/or pleuritis and/or peritonitis.

Sacroiliac joint arthritis: Presence of tenderness on direct compression over the sacroiliac joints.

Spondyloarthropathy: Inflammation of entheses and joints of the lumbosacral spine.

Uveitis: Chronic anterior uveitis as diagnosed by an ophthalmologist.

Use of the Classification in the Published Literature

The ILAR classification requires validation before it is used routinely in the clinical setting. To some extent this process has been advanced by studies already published[2-11], but further challenges remain including evaluation of the requirement of repeated testing of rheumatoid factor, and the development of precisely defined categories that would include all children with chronic inflammatory arthritis of unknown cause.

It is essential that the ILAR classification be used with accuracy. A number of publications appear to have simply substituted the letters JIA for JRA (juvenile rheumatoid arthritis) or JCA (juvenile chronic arthritis), without due attention to the details of inclusion and exclusion criteria. The ILAR criteria represent not only a change in terminology, but in definition. It is important that deviations from

the published criteria are clearly noted, lest they result in inability to interpret and compare the reported data. It is a requirement, for example, for classification in the polyarthritis rheumatoid positive category, that RF be present on 2 occasions at least 3 months apart. This was intended to make certain the unrelated RF positivity, such as that which might follow an infection, not be allowed to obscure what was felt to be significant persistent RF test positivity. This may be contrary to usual clinical practice, and has therefore been an impediment to the easy application of the criteria. Although RF testing would be ideally performed during the first 6 months of disease, this may not always be possible, and test results obtained at a later time should then be used. These requirements should be evaluated; the results of such an evaluation may well influence the criteria. The ILAR committee has concluded that until such data are forthcoming, in keeping with the principles adopted by the committee, the requirement for 2 positive tests for RF will be retained in the present revision.

It is anticipated that the proposed classification will undergo further revision in order to correct anomalies, and in response to new information. Such changes would be incorporated if they resulted in a demonstrable and objective improvement in homogeneity of the categories in the classification. The ILAR classification has proved useful in sparking controversy, questions and international debate, and research about JIA. The prospective gathering of new clinical information has been stimulated and will lead to an improved understanding of these diseases.

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