Classification of Juvenile Idiopathic Arthritis: Should Family History Be Included in the Criteria?

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ABSTRACT. ***Objective.*** (i) To determine the efficacy of the Durban classification for children with juvenile idiopathic arthritis (JIA) where < 5 joints were involved at onset (with systemic arthritis excluded) by determining the proportion of the cohort that proved to be "unclassifiable"; (ii) to define reasons for cases being "unclassifiable," particularly regarding family history; and (iii) to compare the efficacy of a proposed hierarchical system (an unofficial modification of the Durban classification) with the Durban classification, where family history details are included as descriptors, rather than as classification criteria.

Methods. Charts were reviewed of 50 children with fewer than 5 joints involved at presentation for JIA, followed for at least 12 months, with systemic arthritis excluded. Cases were classified according to the EULAR criteria, the Durban criteria, and by a proposed "modified Durban" classification subject to hierarchy, with exclusions in the following order: systemic arthritis, rheumatoid factor (RF) positive arthritis, psoriasis or a combination of dactylitis and psoriatic nail changes (psoriatic arthritis), and HLA-B27 positive arthritis (enthesitis related arthritis), with the remainder of children being classified as having either RF negative polyarthritis or RF negative oligoarthritis, depending on number of joints involved, with additional information noted as descriptors. The "modified Durban" classification was proposed only to stimulate discussion among clinicians.

Results. Of 50 children, 56% were "unclassifiable" by the Durban classification, mainly because of inadequate family history despite appropriate questioning. Using the proposed "modified Durban" classification, 2% were "unclassifiable." Family history was classified as inadequate for the following reasons: The parents did not know family history; the child or parent was adopted; the father was unknown or parent died early; parents never attended; extended family had lost communication with parents; or a relative was considered to have psoriasis, but not confirmed by dermatologists. Other reasons for "unclassifiable" included: dermatologists unable to confirm psoriasis; family history of inflammatory bowel disease and sacroiliitis but B27 status unknown; proband B27 negative but family history of B27-related disease; family history of psoriasis, but patient had insufficient criteria for psoriatic arthritis and therefore excluded from oligoarthritis, psoriatic arthritis and other groups.

Conclusion. (i) The Durban classification showed poor efficacy for JIA where < 5 joints were involved at onset, with more than half the cases being "unclassifiable". (ii) The most common reason was that appropriate family history was not available despite being sought by the clinician. (iii) A proposed hierarchical system, an unofficial modification of the Durban classification, showed good efficacy, with only one of 50 cases being "unclassifiable." (J Rheumatol 2003;30:1857–63)

Key Indexing Terms:
JUVENILE IDIOPATHIC ARTHRITIS ILAR DURBAN
CLASSIFICATION NOMENCLATURE

It is considered that juvenile idiopathic arthritis (JIA) comprises at least 7 different conditions[1], for which there are differing optimal therapeutic regimes, and possibly different etiologies. It has become increasingly relevant to define particular subgroups of JIA with the greatest possible homogeneity, while still providing a classification system that is usable for clinicians. Prior to 1977, there had been few formal recommendations for diagnostic criteria, although there had been at least 3 publications on criteria on JRA between 1971 and 1973[2-4], by the American College of Rheumatology (ACR). In 1977, the European criteria (of the European League Against Rheumatism, EULAR) for juvenile chronic arthritis (JCA)[5] were published. Also in 1977, further North American criteria (ACR)[6] for juvenile rheumatoid arthritis (JRA) were published, and these underwent 2 further revisions in 1986 and 1989. Both the ACR and EULAR criteria defined the 16th birthday as the upper

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age limit at onset. The EULAR criteria for JCA included the spondyloarthropathies and required disease to have been present for 12 weeks. The ACR criteria for JRA excluded the spondyloarthropathies, and required 6 weeks of joint inflammation before diagnosis. The ACR criteria were not included in the current study.

In 1995, an international committee with representatives from Europe, Africa, North and South America, and Asia was convened under the auspices of the International League of Associations for Rheumatology (ILAR) and World Health Organization to review the classification and criteria for childhood arthritis, and a new uniform set of criteria was proposed[1]. These were modified and published in 1997 and have become known as the Durban criteria[7]. These criteria have provided some uniformity for future studies, but need continual modification following informed debate and better understanding of the disease processes.

The ideal classification for research purposes is different from the ideal classification for clinicians, with regard to the amount of detail, the complexity, etc. However, the overall purpose of researchers and clinicians remains the same, that is, better care for children with arthritis. The ideal classification would be a system whereby all cases of childhood arthritis are easily categorized into specific homogenous groups that behave in a standard manner, over the duration of the disease. In practice, this is far from achievable based on the current state of knowledge of JIA.

Studies have shown that difficulties arise in the Durban classification in regard to family history and other problems[8-11]. It was considered worthwhile to define the particular problems encountered in defining the family history and other problems in a cohort of 50 children with arthritis of less than 5 joints at presentation. This would also be helpful in defining how the Durban system might be modified, as well as providing some measures to assess newer classification systems, such as would be proposed following the Task Force meeting in Edmonton in 2001. It was also considered worthwhile for purposes of discussion to look at the Durban system, modified into a hierarchical system, and with family history and laboratory results (other than rheumatoid factor, RF) routinely documented as descriptors.

The proposed "modified Durban" classification[12] (Figure 1) is subject to hierarchy with exclusions in the following order: systemic arthritis, RF positive arthritis, psoriasis or a combination of dactylitis and psoriatic nail changes (psoriatic arthritis), and HLA-B27 positive arthritis (enthesitis related arthritis), with the remainder of children being classified as having either RF negative polyarthritis or RF negative oligoarthritis, depending on the number of joints involved. The only cases that would then be "unclassifiable" would be where it was not possible to exclude categories, i.e., systemic arthritis, RF positive arthritis, psoriatic arthritis, etc. For example, if it could not be decided whether psoriasis was present or absent in a child with arthritis, then this case would be "unclassifiable" because psoriatic arthritis could not be excluded. The modified Durban classification is proposed for the purpose of initiating debate and discussion.

In the modified Durban system[12], it is acknowledged that if the number of involved joints should increase to 5 or more later, then the classification would change; similarly, if the child developed psoriasis or a combination of dactylitis or psoriatic nail changes later, then the classification would change to psoriatic arthritis. Currently, this also occurs within the official Durban classification, where psoriasis, increasing numbers of involved joints, or other manifestations can occur later in a particular child, and change the classification of disease in that child. All classification systems depending on clinical features that can occur independently and serially are likely to exhibit the problem of possible inconsistency of classification over time for one individual.

The objectives of this study were:

1. To determine the efficacy of the Durban classification for children with JIA where less than 5 joints were involved at onset (with systemic arthritis excluded) by determining the proportion of the cohort that proved to be "unclassifiable," i.e., could not be classified in any one subgroup or could be classified in more than one subgroup.
2. To document reasons for disease being "unclassifiable," particularly with regard to family history, with a view to providing a baseline measure for future modifications.
3. To compare the Durban system of classification with a "modified Durban" system of classification, where a simple hierarchy was followed, similar to the Durban system. The family history and additional laboratory details would be noted as descriptors for each proband, with such detail being readily available for research purposes. Detailed and precise information would thus be available on all patients, while clinicians would have a simplified system of defining patients for the purpose of clinical care.

MATERIALS AND METHODS

Charts were reviewed of 50 children with JIA attending or having attended a pediatric rheumatology clinic or the private practice of a pediatric rheumatologist who were documented as having fewer than 5 joints involved at presentation, whose arthritis had been followed for at least 12 months. The family history data were collected prospectively. Cases of systemic arthritis were excluded. The following data were extracted: number of joints involved before 6 months and at 12 months, the presence of family history of psoriasis and whether confirmed by a dermatologist, presence of family history of HLA-B27 associated disease and whether medically confirmed, the presence of positive test for RF, and B27 antigen. The cases were classified according to the EULAR criteria, and the Durban criteria. They were also classified by a proposed "modified Durban" classification that is subject to simple hierarchy (Figure 1). In this proposed classification in hierarchical order, exclusions are (1) systemic arthritis, (2) RF positive arthritis, (3) psoriatic arthritis (i.e., arthritis and psoriasis, or arthritis and a combination of dactylitis and psoriatic nail changes), (4) enthesitis related arthritis (arthritis and HLA-B27 positive after exclusions as above), with the remainder of the patients being classified as having

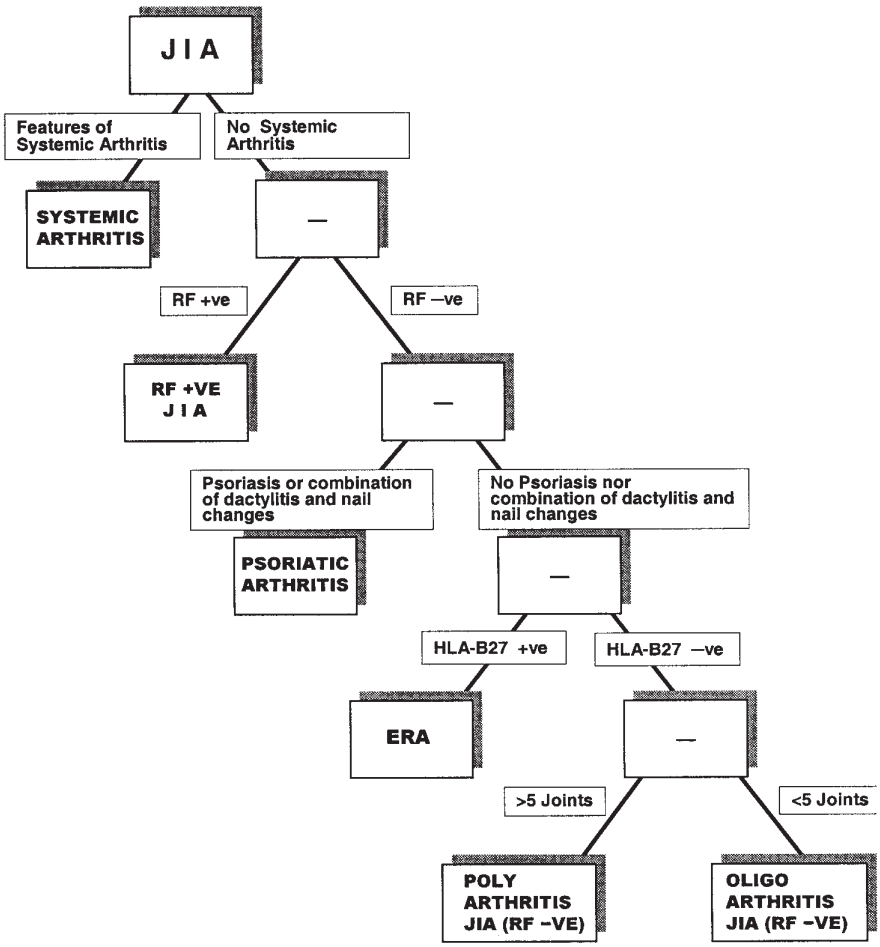

Figure 1. Hierarchical classification of juvenile idiopathic arthritis (JIA), "modified Durban" classification. RF: rheumatoid factor, ERA: enthesitis related arthritis.

either (5) RF negative polyarthritis or (6) RF negative oligoarthritis, depending on whether there were 5 or fewer joints involved. A case was considered "unclassifiable" if it was categorized into "other arthritis" where the particular case did not fit the criteria for any defined subgroup or fitted into more than one subgroup.

Every effort was made to obtain all relevant information from the parents regarding family history. Where parents were not able to provide information specifically excluding medically confirmed psoriasis or HLA-B27 positive disease in relatives due to reasons such as father's identity unknown or child adopted, that particular case was considered "unclassifiable," as this information would never become available. It is the interpretation of the authors that since certain aspects of family history are diagnostic criteria, if this information is not available then it is not possible to classify according to the criteria. Where the parents were able to reasonably estimate whether the above conditions were present or not, this information was taken to be correct, although the accuracy of this should be tested in future studies.

RESULTS

The diagnoses of 50 children according to the 3 sets of criteria are listed in Table 1; patient details are listed in Table 2. Of 50 children presenting with less than 5 joints involved, at least 20 were classified prior to the publication of the Durban system of classification. Of these, 15 had not been tested for RF, and given the course of the disease, there had been no clinical indication at the time to investigate for RF, outside of classification considerations. This would make these cases "unclassifiable" by the Durban system, and also by the proposed "modified Durban" system. However, clinically it was very unlikely these children would have had RF, particularly where there were less than 4 joints involved. In addition, the 15 children had relatively mild disease, and at the time of submission of this report these children were no longer under the care of the rheumatologists. This was further evidence that these children were very unlikely to have been RF positive. arthritis the 15 children Details of the 15 children are included in Table 2. To better estimate the usefulness of the classification criteria in prospective studies where information on RF would be readily available, the data on these 15 children were analyzed presuming them to be RF negative at the time of disease.

An attempt was then made to find all 15 children and to test for the presence of RF. Eventually, 10 were located and

Table 1. Diagnoses of 50 children by 3 sets of criteria.

EULAR Criteria	n	Durban Criteria	n	"Modified Durban" Criteria	n
Juvenile ankylosing spondylitis	7	Enthesitis related arthritis	1	Enthesitis related arthritis	7
Pauciarticular JCA	37	Persistent oligoarticular JIA	16	Oligoarthritis, RF negative	36
Pauci to Poly JCA	5	Extended oligoarticular JIA	3	Polyarthritis, RF negative	5
Psoriatic	1	Psoriatic	2	Psoriatic	1
		"Unclassifiable"	28	"Unclassifiable"	1
Total	50		50		50

Pauci to Poly: Pauciarticular becoming polyarticular; JCA: juvenile chronic arthritis; JIA: juvenile idiopathic arthritis; RF: rheumatoid factor.

proved to be RF negative. Five were not located. While this does not absolutely prove that the children were negative for RF at the time of the disease, it provides further evidence that this was very likely to be so. It is well known that children with RF positive disease tend to have serious persisting disease that seldom converts to seronegativity unless aggressive therapeutic interventions are used. This was not the case for these 10 children.

Presuming the RF to be negative for these 15 children where it was not tested originally, by the Durban classification (reasons justifying this as above), 28 children (56%) were "unclassifiable." Using the proposed "modified Durban" classification, one child (2%) was "unclassifiable."

Of the "unclassifiable" by the Durban criteria:

1. Eighteen patients (36%) had insufficient family history of B27 associated disease or psoriasis. The reasons given for this included: the parents claimed no knowledge of family history; the child or one parent was adopted; the father was unknown; the child attended only with foster parents; one parent had died early or aunts, uncles, and grandparents had not communicated with the patient's parents for many years. (See reasons A and B in Table 2) Of these 18 (36%), 2 (4%) had an additional reason for being "unclassifiable."
2. Six patients (12%) had definite family history of psoriasis, but insufficient criteria to fulfil criteria for psoriatic arthritis. (See reason C in Table 2) Of these 6 (12%), 2 (4%) had an additional reason for being unclassifiable.
3. One patient (2%) was unclassifiable because the rash could neither be diagnosed by a dermatologist as psoriasis nor excluded. (See reason D in Table 2)
4. One patient (2%) was B27 negative, but had a definite family history of B27 positive associated disease. No category is suitable for this case. (See reason E in Table 2)
5. Four patients (8%) were unclassifiable because there was a definite family history of psoriasis but a dermatologist had not been involved. (See reason F in Table 2) Of these 4 (8%), 2 (4%) had an additional reason for being unclassifiable.
6. One patient (2%) was unclassifiable because the features fulfilled the criteria for 2 subgroups, enthesitis related arthritis and persistent oligoarthritis. (See reason G in Table 2)

Of the "unclassifiable" by the modified Durban criteria, the disease of only one child was unclassifiable where a dermatologist was not able to diagnose psoriasis or exclude it.

DISCUSSION

The proportion of children with "unclassifiable" disease in the Durban system is large in this cohort, the most common reason being inadequate information on family history. For this study, the family history was considered to be inadequate only for the reasons listed in Results (above). Since the family history was collected prospectively, the missing information was not because of inadequate history taking, but because the information was not available and could not be accessed.

The proportion of "unclassifiable" cases in our study is greater than in previous studies[3,4,6,8], where family history has nevertheless consistently been identified as a problem. The reasons for the larger proportion include the following: (1) In our study very strict criteria have been applied regarding quality of information about family history, e.g., if a first-degree relative has a scaling rash of unknown diagnosis then the proband is strictly unable to be categorized. (2) Family history has been probed deeply, and issues of unknown paternity and other sensitive matters have been revealed.

Notable in Table 1 is the similarity in the classification according to the EULAR criteria and the "modified Durban"[12] with regard to proportion of cases in each group. Both classifications have been described in detail above. The modified Durban is more precise than the EULAR. However, it happens that in the current cohort of patients, all with fewer than 5 joints involved at presentation, the classification results are similar. The only case that was different was the child who had a rash that could not be diagnosed, and therefore was undiagnosable in the "modified Durban" system.

A potential problem beyond the scope of this study is assessment of accuracy of family history as given by the parent or patient. It is unproven whether accuracy is related to intelligence and understanding of the parents, their degree

Table 2. Details of patients.

Patient	Sex	B27	RF	FH, B27 disease	Med Confirmed	Psoriasis	FH Psoriasis	Derm Confirmed	EULAR	Durban	Reason for U, Durban†	Modified Durban	Reason for U, Mod Durban
1	M	1	3*	1	1	2	1	1	JAS	U	C	ERA	
2	F	1	3*	1	1	2	1	1	JAS	U	C	ERA	
3	M	2	2	2		2	3		Pauci	U	B	Oligo RF–	
4	F	2	2	3		2	2		Pauci	U	A	Oligo RF–	
5	F	2	3	2		2	2		Pauci	P. Oligo		Oligo RF–	
6	F	2	2	2		2	2		Pauci to poly	E. Oligo		Poly RF–	
7	M	1	2	2		2	2		JAS	ERA		ERA	
8	F	2	2	2		2	2		Pauci	P. Oligo		Oligo RF–	
9	M	2	2	2		1			PsA	PsA		PsA	
10	F	2	3	3		3	3		Pauci	U	AC	Oligo RF–	
11	M	2	2	3		2	2		Pauci	U	A	Oligo RF–	
12	F	2	3*	3		2	2		Pauci	U	A	Oligo RF–	
13	F	2	2	2		3	2		Pauci	U	D	U	D
14	F	2	3*	2		2	2		Pauci	P. Oligo		Oligo RF–	
15	F	2	3	2		2	2		Pauci	P. Oligo		Oligo RF–	
16	F	2	2	2		2	2		Pauci to poly	E. Oligo		Poly RF–	
17	F	2	2	3		2	2		Pauci	U	A	Oligo RF–	
18	F	2	3*	2		2	2		Pauci	P. Oligo		Oligo RF–	
19	F	2	3*	2		2	2		Pauci	P. Oligo		Oligo RF–	
20	F	2	3*	2		2	1	3	Pauci	U	F	Oligo RF–	
21	M	2	3*	2		2	3		Pauci	U	B	Oligo RF–	
22	F	2	3	2		2	2		Pauci	P. Oligo		Oligo RF-	
23	F	2	2	3		3	3		Pauci to poly	U	AB	Poly RF–	
24	F	2	2	2		2	2		Pauci	U	CF	Oligo RF–	
25	F	1	2	2		2	2		JAS	U	G	ERA	
26	F	2	3	2		2	2		Pauci	P. Oligo		Oligo RF–	
27	M	2	2	1	1	2	2		Pauci	U	E	Oligo RF–	
28	F	2	2	3		2	3		Pauci	U	AB	Oligo RF–	
29	M	2	2	3		2	3		Pauci	U	AB	Oligo RF–	
30	M	2	3*	3		2	3		Pauci	U	AB	Oligo RF–	
31	M	2	2	2		2	2		Pauci	P. Oligo		Oligo RF–	
32	M	2	2	3		2	3		Pauci	U	AB	Oligo RF–	
33	F	2	2	2		2	2		Pauci	P. Oligo		Oligo RF–	
34	F	2	2	2		2	2		Pauci	P. Oligo		Oligo RF–	
35	F	2	3*	2		2	2		Pauci	P. Oligo		Oligo RF–	
36	M	2	2	2		2	2		Pauci	P. Oligo		Oligo RF–	
37	F	2	2	2		2	3		Pauci	U	B	Oligo RF–	
38	M	2	2	3		2	3		Pauci	U	B	Oligo RF–	
39	F	2	2	2		2	2		Pauci to poly	P. Oligo		Poly RF–	
40		2	2	2		2	1	2	Pauci	U	F	Oligo RF–	
41	M	1	2	1	3	2	1	1	JAS	U	C	ERA	
42	M	2	2	2		2	3		Pauci	U	B	Oligo RF–	
43	F	2	2	2		2	2		Pauci to poly	E. Oligo		Poly RF–	
44	F	1	2	3		2	3		JAS	U	AB	ERA	
45	M	2	2	2		2	1	1	Pauci	U	C	Oligo RF–	
46	F	2	2	2		2**	1	1	Pauci	PsA		Oligo RF–	**
47	F	2	2	2		2	2		Pauci	P. Oligo		Oligo RF–	
48	F	2	2	2		2	2		Pauci	P. Oligo		Oligo RF–	
49	M	1	2	3		2	2		JAS	U	A	ERA	
50	F	2	2	3		2	1	3	Pauci	U	AF	Oligo RF–	

1 positive; 2 negative; 3 unknown. Med. Confirmed: medically confirmed. Derm. Confirmed: A diagnosis of psoriasis in family confirmed by dermatologist. Reason for U, Durban: Reason for being "unclassifiable" by the Durban criteria. Reason for U, Mod. Durban: Reason for being "unclassifiable" by the modified Durban criteria. U: unclassifiable; RF: rheumatoid factor. Pauci: pauciarticular onset JCA. Pauci to Poly: Pauciarticular onset JCA becoming polyarticular JCA. JAS: juvenile ankylosing spondylitis. P. Oligo: persistent oligoarthritis. Oligo RF–: oligoarthritis, RF negative. PsA: psoriatic arthritis. ERA: enthesitis related arthritis. * Later tested for presence of RF and found to be negative. ** The presence of nail pits and family history of psoriasis makes the classification differ between Durban and "modified Durban." The "modified Durban" does not include family history in criteria, and hence did not fulfil criteria for psoratic arthritis in "modified Durban." † Listed reasons for proband being "unclassifiable": A: Family history for B27 associated disease inadequate. B: Family history of psoriasis inadequate. C: Family history positive for psoriasis but not present in proband, and insufficient to fulfil criteria for psoriatic arthritis in proband. D: Dermatologist was unable to be definite about diagnosis of psoriasis in proband. E: Proband known to be B27 negative, relative with proven B27 associated disease, and insufficient to fulfil criteria for ERA in proband, but excluded from oligoarthritis. F: Definite psoriasis in family, but not diagnosed by dermatologist. G: Proband had sufficient criteria to fulfil 2 categories (ERA, persistent oligoarthritis).

of concern about the family history, mastery of the language, and a number of other social issues.

It is known that families are sometimes unaware of the existence of certain family members, e.g. half-siblings, who may have relevant medical conditions such as psoriasis that could change the classification. Inaccuracies in family history may also occur due to issues of mistaken paternity and other such problems. These questions should be addressed in further studies.

Family history is particularly relevant in first-degree relatives such as siblings. If the proband is an only child, the opportunity for a significant amount of family history in siblings is not present. Further studies are required to determine whether the existence or nonexistence of siblings (i.e., the existence or nonexistence of potential positive family history of relevant disease) significantly changes the potential classification where family history is included in classification criteria. For example, one child may have JIA that is classified as psoriatic arthritis because among other things, one sibling has psoriasis. Another child, with identical disease but with no siblings, may be classified differently because no siblings exist and there is no other family history of psoriasis in a first-degree relative.

Relevant conditions in the family history including chronic disease of the musculoskeletal system may manifest later or remain undiagnosed. Hence, the recorded family history for the proband may be inaccurate since it is changeable. This would suggest that for the Durban classification to remain accurate for each case, family history for every proband would need to be continually updated, and the classification adjusted appropriately if a family member later develops a relevant condition such as psoriasis. This issue should also be addressed in future studies. It should be noted that such changes in classification due to late manifestation of clinical features influence both the Durban classification and the proposed "modified Durban" classification.

The quality and quantity of family history revealed may be dependent on the biases, determination, and skill of the questioning physician. This should be the subject of future studies in order to standardize methods of collection of family history, if this information is to be used as classification criteria.

There are many unanswered questions about family history — the accuracy, the completeness, the comparability of the quality, the changing nature of it, etc. The influence of these factors should be scientifically assessed before they can be incorporated in any classification system that aims to be precise enough for quality research. It is questionable whether family history can ever be sufficiently accurate for this purpose, particularly when the areas of interest in the family history are chronic musculoskeletal conditions well known to be poorly diagnosed in many communities. It should be noted that the presence of an undiagnosed "scaling" rash in family members would make JIA in any proband "unclassifiable."

In the "modified Durban" system we propose, where family history is recorded in descriptors, not criteria, the disease of only one of 50 children could not be classified, due to the dermatologist being unable to exclude a diagnosis of psoriasis in the proband. It would seem appropriate that this child's condition should remain unclassified until a diagnosis of the rash was possible. The disease of all other children was able to be classified, with the family history recorded as descriptors. Thus no information was lost.

With regard to the suggested hierarchical system of classification, it is simple and precise and easy for clinicians to use. It is important that this should be so, since not only does therapy depend on accurate classification, but all research begins with accurate classification by a clinician. Hence researchers and clinicians must share an effective and workable classification.

This study highlights the many difficulties of including family history in classification criteria, including many causes and potential causes of inaccuracies. It has highlighted a number of issues that should be studied further regarding the accuracy of family history when used in classification criteria.

This study would suggest that until these issues have been adequately addressed, it may be inappropriate to include family history as part of the criteria for any classification system of childhood arthritis. A "modified Durban" classification is presented and compared with the Durban classification. It should be noted that the former is presented for purposes of discussion and debate and has no official status.

In summary: The Durban classification showed poor efficacy for JIA where less than 5 joints were involved at onset, with more than half the cases being "unclassifiable." The most common reason was that appropriate family history was not available, despite it being sought by the physician. A proposed hierarchical system, a modification of the Durban classification, showed good efficacy, with only one of 50 cases being "unclassifiable" without the loss of relevant information, particularly family history, which was recorded in descriptors.

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