PRELIMINARY CRITERIA FOR THE CLASSIFICATION OF THE ACUTE ARTHRITIS OF PRIMARY GOUT

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The American Rheumatism Association subcommittee on classification criteria for gout analyzed data from more than 700 patients with gout, pseudogout, rheumatoid arthritis, or septic arthritis. Criteria for classifying a patient as having gout were a) the presence of characteristic urate crystals in the joint fluid, and/or b) a tophus proved to contain urate crystals by chemical or polarized light microscopic means, and/or c) the presence of six of the twelve clinical, laboratory, and X-ray phenomena listed in Table 5.

Acute gouty arthritis has been clinically recognized since antiquity. Nevertheless comparisons of studies of the natural history of gout, of the evaluation of therapy, and of the epidemiology of the disorder have suffered from the lack of a standard classification. In an attempt to achieve a more uniform system for reporting and comparing data, a subcommittee of the Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association was charged with assembling information, so that criteria for the classification of arthritis due to primary gout could be developed.

From the Gout Classification Criteria Subcommittee of the American Rheumatism Association Committee on Diagnostic and Therapeutic Criteria.

Supported in part by The Arthritis Foundation, by PHS Research Grant AM-12049 from the NIAMDD, and by the Jonathan Joseph Research Foundation.

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Submitted for publication November 8, 1976; accepted November 24, 1976.

DATA COLLECTION

Rheumatologists in teaching clinics and in private practice collected data on patients with the following diagnoses: primary gout; definite or classic rheumatoid arthritis (RA) (1) of 2 years or less duration; definite or classic RA of more than 2 years duration; pseudogout; and acute septic arthritis (other than tuberculosis). Thirty-eight rheumatologists from 38 centers distributed across the United States contributed data on up to 5 patients in each category. The following numbers of acceptable protocols were submitted: gout—178, RA $\leq$ 2 years duration—143, RA $>$ 2 years duration—156, pseudogout—110, and acute septic arthritis—119, yielding a total of 706 patients for analysis. Contributors were selected by the committee on the basis of interest in and experience with gout and its differential diagnosis.

It must be noted here that no information was collected on patients with secondary gout. All subsequent conclusions to be drawn from the data can only be applied to primary gout. In addition, no control groups consisting of patients with degenerative joint disease, Reiter's syndrome, psoriatic arthritis, etc, were used in the study. The comparisons to be made are between acute gout and the specified control diseases.

The data reporting form designed by the committee included seven pages of questions relating to the details of

onset and joint involvement during the first attack (or beginning of arthritis) as well as the most recent attack, if different from the first episode or onset. In addition, questions were asked about family history of gout, evidence of renal calculi, factors precipitating attacks, response to colchicine therapy, laboratory findings including serum uric acid, rheumatoid factor, tests of renal function, joint fluid analysis, and joint X rays. Distribution of joint involvement was noted. All forms were reviewed for accuracy and completeness by the committee chairman (SLW). Some were returned to the contributors because of internal inconsistencies. Only those forms considered to demonstrate the claimed diagnosis and to have consistent data, whether or not all details were available, were accepted for analysis.

METHODS OF ANALYSIS

From 53 items on the form, 205 dichotomous and 30 continuous variables were created for analysis of the patients in the different diagnostic groups. Most of the items from the history and physical exam were analyzed according to first attack, most recent attack, or either attack. Data were coded for computer processing, with noncontinuous variable responses recorded as present, absent, or not known. If there was no response to a particular question, the information was coded as not known. In subsequent analyses the not known entries either were not included or were assigned values, i.e. present or absent, according to a program of random allocation of results as described below. Continuous data were coded directly, but for some variables, such as serum uric acid determinations performed in different laboratories, consideration was given to differences in the upper limits of normal. Thus the highest uric acid value was coded directly, and analyzed both as an absolute value and in relation to the upper limit of normal for that method in that laboratory. Serum uric acid levels were also analyzed as a dichotomous variable: normouricemia/hyperuricemia. Hyperuricemia was defined separately for each laboratory as a level above the mean plus two standard deviations from the mean uric acid level for a healthy population, by the method used.

Table 1. *Proposed Criteria for Acute Arthritis of Primary Gout*

1. More than one attack of acute arthritis
2. Maximum inflammation developed within 1 day
3. Monoarthritis attack
4. Redness observed over joints
5. First metatarsophalangeal joint painful or swollen
6. Unilateral first metatarsophalangeal joint attack
7. Unilateral tarsal joint attack
8. Tophus (proven or suspected)
9. Hyperuricemia
10. Asymmetric swelling within a joint on x ray*
11. Subcortical cysts without erosions on x ray
12. Monosodium urate monohydrate microcrystals in joint fluid during attack
13. Joint fluid culture negative for organisms during attack

* This criterion could logically be found on examination as well as on x ray. However the protocol did not request this information in regard to examination.

Table 2. *Proposed Survey Criteria for Acute Arthritis of Primary Gout*

1. More than one attack of acute arthritis
2. Maximum inflammation developed within 1 day
3. Oligoarthritis attack
4. Redness observed over joints
5. First metatarsophalangeal joint painful or swollen
6. Unilateral first metatarsophalangeal joint attack
7. Unilateral tarsal joint attack
8. Tophus (proven or suspected)
9. Hyperuricemia
10. Asymmetric swelling within a joint on x ray*
11. Complete termination of an attack

* This criterion could logically be found on examination as well as on x ray. However the protocol did not request this information in regard to examination.

The committee recognized that not all the variables were independent. Analysis of over 200 variables in five study groups totaling over 700 patients had to be simplified in a rational fashion, to yield a more limited number of criteria, which could then be applied to the classification of the acute arthritis of primary gout. First it was decided to identify those individual variables that best discriminated the study groups, then to select the fewest possible which, when totaled, would allow acceptable sensitivity and specificity for classification. Sensitivity was defined as the proportion of patients with primary gout fulfilling proposed criteria. Specificity was defined as the proportion of control patients that did not fulfill proposed criteria.

Each variable was analyzed in terms of its probability of occurrence in the study groups by series of χ^2, t, and analysis of variance tests. At least half the variables showed some degree of statistical difference by these analyses. Further selection of variables was based on the overall degree of discrimination observed, as well as on clinical judgment regarding the degree of independence of the selected variables. Only the most discriminatory of related variables was used. Multivariate analysis was used to verify that variables selected for consideration as criteria contributed significantly to the classification of acute gout compared to the other disease groups. In addition, variables of high specificity but low sensitivity (e.g. renal stone), or with a paucity of information in control groups (e.g. response to colchicine) were not selected. By such processes, each committee member selected 10 variables that seemed best to discriminate gout from the other disorders. The composite list was reviewed for duplication, and by a process of committee evaluation, 13 criteria were chosen. These criteria are listed in Table 1.

The problem of incomplete data was considered at great length by the committee. A final decision was made to allocate missing information randomly, in proportion to its presence or absence in the patients in whom appropriate information was available. No method of coping with missing data is ideal, but random allocation allows maximal data utilization on all patients, and tends to allow for optimal sensitivity of the criteria. In any system in which classification depends upon the presence of a specified number of criteria, incomplete data in a patient means that each missing variable cannot be counted

Table 3. *Clinical Features of Primary Gout and Control Patients*

Clinical Features	Primary Gout (n = 178)	Pseudo-gout (n = 110)	RA ≤ 2 Years (n = 143)	RA> 2 Years (n = 156)	Septic Arthritis (n = 119)
Women (%)	13.6	54.6	64.3	64.1	51.3
Joint fluid examined for crystals (%)	50.6	82.7	21.0	26.3	70.6
Mean age (years)	56.2	68.8	47.6	52.2	38.3
Duration of disease (years)	10.1	6.3	1.2	11.0	—

toward the necessary number. The net effect is the same, under those circumstances, as if the patient were known to be negative for the variable.

A related list of criteria (Table 2) was developed to be used in a single patient visit to a clinic or office, or in population surveys by history and review of clinic records. Joint aspiration was not required for these criteria. The survey criteria were analyzed separately in order to evaluate their sensitivity and specificity in the classification of acute arthritis of primary gout.

RESULTS

The sex distribution and the mean values for age and duration of disease for each of the five groups are shown in Table 3 for the 706 patients accepted for analysis. As might be expected, the gout group had the lowest proportion of females (13.6%). It was particularly interesting that only about half (50.6%) of the gout patients, seen by academic rheumatologists with a particular interest in gout, had their joint fluid examined for crystals, in comparison to nearly 25% of the rheumatoid patients and more than 80% of pseudogout and 70% of septic arthritis patients. The reason for the relative infrequency of joint aspiration in the patients with acute gout was not clear. In part it may be because inflamed tarsal and interphalangeal joints are difficult to aspirate.

Of the 90 patients with gout who had joint fluid examinations, characteristic microcrystals of sodium urate monohydrate were seen in synovial fluid in 76 (84.4%). No urate crystals were seen in any of the other disease groups (Table 4). The crystals were defined by needle or rod shape and by negative birefringence. Questions were asked about extinction angle and about digestion of the crystal by uricase; this information was often not available.

A proven tophus was defined as a mass of variable size, grossly demonstrable in body tissues by physical diagnostic techniques, and which was proved to contain sodium urate crystals either chemically or by polarized light microscopy. A suspected tophus was defined as a subcutaneous or intracutaneous mass, exhibiting white to yellowish content, which was not tested for sodium urate crystals. The location of the suspected tophus was described, and in all cases was found in typical sites. The presence or absence of proven tophus could be established in 172 patients with gout, all with rheumatoid arthritis and pseudogout, and in 112 of the 119 patients with septic arthritis. Proven tophus, as defined, was found in 52 of 172 patients with gout, in none of those with rheumatoid arthritis or with pseudogout, and in 4 patients with septic arthritis. These data are summarized in Table 4.

The presence of urate crystals in joint fluid was a moderately sensitive classification criterion for acute gout, being found in 84.4% of patients with gout in whom joint fluid was analyzed. The reasons for the failure to find crystals in the remaining patients are not certain. The skill of the searcher and the vigor with which crystals were looked for are variables that were not studied. The patients in whom crystals were not found were not clinically different from the rest of the population of gouty patients. The overwhelming value of the crystal criterion lies in its absolute specificity; no patient with rheumatoid arthritis, septic arthritis, or pseudogout showed urate crystals.

Table 4. *Urate Crystals in Joint Fluid and Proven Tophi*

	Primary Gout (n = 178)	Pseudo-gout (n = 110)	RA ≤ 2 Years (n = 143)	RA > 2 Years (n = 156)	Septic Arthritis (n = 119)
Urate crystals	76 of 90	0 of 91	0 of 30	0 of 41	0 of 84
Proven tophi	52 of 172	0 of 110	0 of 143	0 of 156	4 of 112

Table 5. *Percentage Distribution of Positive Responses and Number of Specified Responses to Individual Criteria Among Diagnostic Groups*

Individual Criteria	Primary Gout (n = 178)	Pseudo-gout (n = 110)	RA ≤ 2 Years (n = 143)	RA > 2 Years (n = 156)	Septic Arthritis (n = 119)
Maximum inflammation 1 day	85.1 (154)*	59.8 (82)	12.1 (124)	10.7 (122)	32.3 (93)
More than one attack	86.5 (178)	71.7 (106)	36.2 (141)	58.1 (155)	11.8 (119)
Monoarticular arthritis	71.9 (178)	63.6 (110)	13.3 (143)	9.6 (156)	49.6 (119)
Redness	92.2 (166)	51.0 (102)	38.5 (122)	43.9 (130)	75.0 (108)
First MTP pain or swelling	78.0 (173)	6.8 (103)	32.4 (142)	44.7 (152)	3.4 (118)
Unilateral first MTP	47.1 (174)	0.9 (108)	8.8 (137)	9.0 (156)	1.7 (119)
Unilateral tarsal	21.1 (171)	1.9 (108)	5.1 (137)	5.8 (156)	5.0 (119)
Suspected tophus	19.5 (108)	1.0 (101)	0 (139)	0 (152)	0.9 (108)
Hyperuricemia	92.2 (167)	17.5 (97)	11.0 (90)	9.3 (97)	18.4 (77)
Asymmetric swelling	41.9 (117)	13.3 (83)	8.0 (113)	11.5 (130)	20.2 (99)
Subcortical cysts, no erosions	11.9 (126)	2.0 (99)	2.5 (118)	3.4 (145)	1.0 (102)
Negative organisms on culture	95.9 (49)	96.5 (57)	100.0 (14)	100.0 (20)	24.0 (104)

* Numbers in parentheses indicate the number of individuals with each disorder on whom information was available for each criterion.

Proven tophi were less sensitive, being found only in about 30% of patients with gout. However proven tophi were nearly as specific as urate crystals; fewer than 1% (4 of 521) of the control group had tophaceous deposits. Presumably these four positive patients had both tophaceous gout and septic arthritis. Their acute episodes might have been misclassified as acute gout, rather than as septic arthritis, if proven tophus had been considered as an absolute criterion.

It seems reasonable, therefore, to consider urate crystals in the joint fluid as an absolute criterion enabling the classification of any patient with the appropriate crystals in the joint fluid as having acute gout. Other rheumatic diseases may occasionally coexist with acute gout, although none was seen in this study.

Proven tophus is both less sensitive and less specific than joint fluid crystals. Although not an absolute criterion, proven tophus, when present, nevertheless seems to be most useful in distinguishing acute gout from the control disorders. This criterion is 30% sensitive and 99% specific (against the totality of control disorders).

There were 102 individuals with primary gout in this study in whom joint fluid urate crystals were either not searched for or not found when sought. Of those with primary gout, 126 did not have proven tophi as described above, and 71 had neither demonstrable crystals nor tophi. Clearly a further set of classification criteria is necessary to distinguish acute gout from the control diseases. Table 5 reports the information collected in regard to the other twelve criteria, including suspected tophus, in all patients with acute gout, pseudogout, rheumatoid arthritis, and septic arthritis. This table shows the percentage of patients in each group that had each criterion. The variable suspected tophus excludes those patients with proven tophi; in all other respects every individual on whom information is available is included in this analysis.

Table 6. *Number and Percentage of Patients in Each Disease Group with Selected Numbers of Positive Criteria*

Disease Group	No. of Patients	Positive Criteria* 5 or More No.	5 or More %	6 or More No.	6 or More %	7 or More No.	7 or More %
Primary gout	178	170	95.5	156	87.6	132	74.1
Pseudogout	110	30	27.3	12	10.9	3	2.7
RA ≤ 2 years	143	10	7.0	4	2.8	0	0.0
RA > 2 years	156	13	8.3	2	1.3	1	0.6
Total RA	299	23	7.7	6	2.0	1	0.3
Septic arthritis	119	8	6.7	3	2.5	1	0.8

* Criteria are those listed in Table 5.

Table 7. *Number and Percentage of Patients in Each Disease Group with Selected Numbers of Positive Survey Criteria*

Disease Group	No. of Patients	Positive Criteria: 5 or More No.	%	6 or More No.	%	7 or More No.	%
Primary gout	178	168	94.4	151	84.8	116	65.2
Pseudogout	110	28	25.5	8	7.3	2	1.8
RA ≤ 2 years	143	6	4.2	2	1.4	0	0.0
RA > 2 years	156	18	11.5	3	1.9	1	0.6
Total RA	299	24	8.0	5	1.7	1	0.3
Septic arthritis	119	8	6.7	3	2.5	1	0.8

Table 6 shows the number and percentage of patients within each disease group who had five or more, six or more, or seven or more positive criteria from among the twelve criteria listed in Table 5. Five or more criteria were found in 95.5% of patients with primary gout, and in 6.7–8.3% of patients with septic or rheumatoid arthritis. However 27.3% of patients with pseudogout also satisfied five criteria, an unacceptable lack of specificity. Six or more of these criteria were found in 87.6% of patients with acute primary gout, and in only 1.3–2.8% of those with septic arthritis or rheumatoid arthritis. Nearly 11% of patients with pseudogout satisfied six or more criteria. The requirement of seven criteria reduced the sensitivity in acute gout to 74.1%, but improved the specificity greatly; only 2.7% of patients with pseudogout and less than 1% of those with other control disorders had seven criteria.

When urate crystals in the joint fluid and/or proven tophus are excluded, the best combination of specificity and sensitivity seems to be with six of the twelve criteria listed in Table 5.

The presence of crystals, proven tophi, and/or combinations of the various criteria from Table 5 in our patients with gout has been evaluated. At the six-or-more criteria level from Table 5, when urate crystals and proven tophi were considered, 97.8% of gout patients satisfied one or more of these methods of classification.

The related survey criteria recorded in Table 2 were also analyzed. These criteria include tophus (proven or suspected), but not subcortical cyst without erosion on X ray, urate crystals in joint fluid, or joint fluid culture negative for organisms. Oligoarthritis has been substituted for monoarthritis and complete termination of an attack has been added. The total is eleven criteria. Table 7 records the number and percentage of patients in each disease group who had five or more of these criteria. Six of the eleven criteria would have to be present to produce acceptable sensitivity and specificity.

DISCUSSION

The best way to classify a patient as having acute gout is to demonstrate characteristic sodium urate monohydrate crystals in the joint fluid. This survey of actual practices among rheumatologists interested in gout demonstrates the difficulties in restricting oneself to this single criterion. Crystals were actually sought at any time in the patient's course in only about half of the patients with acute gout in this study. When searched for, characteristic crystals were found in acute gout only 85% of the time. Schumacher *et al* (2) have recently reported a group of patients with acute gouty arthritis in whom crystals were sought and not found, and they have discussed in detail possible reasons for this failure.

The presence of tophi, proved to contain sodium urate crystals either chemically or by polarized light microscopy, also has been shown by this study to be useful in categorizing patients. It must be remembered that every patient entered into the project had articular inflammation of some sort. Gout may infrequently coexist with acute septic arthritis (3,4), acute pseudogout (4,5), or active rheumatoid arthritis (6). In this study simultaneous proven tophaceous gout and a second articular disorder were established in only 4 patients with septic arthritis. Another patient with septic arthritis and one with pseudogout had suspected tophi. For these reasons the presence of a proven tophus cannot be an absolute criterion that the associated acute arthritis is gouty. Nevertheless, although sensitivity was low, the specificity of proven tophus for acute gout was very high (over 99% totally, and over 96% against septic arthritis).

In the absence of either joint fluid or tophaceous sodium urate crystals, the remaining clinical, radiologic,

and laboratory criteria listed in Table 1 (and in Table 5) served as reasonable classification criteria for acute gouty arthritis. Six or more criteria from this list of twelve were found in 87.6% of patients with gout, in 10.9% of patients with acute pseudogout, and in much smaller percentages of the other control disease patients. The combination of crystals, tophi, and/or six or more of the clinical, x-ray, and laboratory criteria was highly sensitive; it identified 97.8% of our patients with gout.

The proposed survey criteria listed in Table 2, ascertainable in a single patient visit or by history and review of clinic records, required the presence of six of eleven criteria to produce a somewhat greater specificity (92.7% against pseudogout) and lower sensitivity (84.8%) than the six of twelve criteria described above. However these criteria were chosen specifically to be useful in population surveys, and it seems appropriate to test them in the future in such an investigation.

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