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Preliminary Criteria for Classification of Adult Still's Disease

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Abstract. **We have attempted to design classification criteria for adult Still's disease by analyzing the data obtained through a multicenter survey of 90 Japanese patients with this disease and of 267 control patients. The proposed criteria consisted of fever, arthralgia, typical rash, and leukocytosis as major, and sore throat, lymphadenopathy and/or splenomegaly, liver dysfunction, and the absence of rheumatoid factor and antinuclear antibody as minor criteria. Requiring 5 or more criteria including 2 or more major criteria yielded 96.2% sensitivity and 92.1% specificity. However, an exclusion process will be needed for an accurate classification, since this disease is relatively rare. (*J Rheumatol 1992;***19:424–30)**

Key Indexing Terms:
ADULT STILL'S DISEASE CLASSIFICATION CRITERIA

Adult Still's disease is one of the febrile disorders of unknown etiology, characterized by typical spiking fever with evanescent rash and the involvement of various organs[1,2]. Because this disease almost lacks specific clinical, laboratory, and histological features, a physician often has difficulty making a definite diagnosis, especially for an early stage case. There have never been well validated criteria for diagnosis or classification of this disease, established through a statistical process. However, several authors[3-6] have proposed their own diagnostic criteria without a statistical endorsement such as demonstration of sensitivity and specificity.

The Adult Still's Disease Research Committee was organized in 1987 in Japan to accurately characterize the clinical picture of this disease and also to prepare the classification criteria. The results of a multicenter survey of Japanese patients were already published[7]. By using these data and also the data obtained similarly through a multicenter survey of the control patients, we have attempted to prepare the classification criteria of adult Still's disease in a statistically based manner.

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MATERIALS AND METHODS

The Adult Still's Disease Research Committee consisted of 11 individuals who are shown as authors of this article. The clinical data on 90 patients with definite adult Still's disease were derived from our previous work[7] in which a detailed process of classifying the definite cases was mentioned. Briefly, by the questionnaire method performed from April, 1988 through May, 1989, detailed information concerning 39 clinical items on 146 Japanese patients with adult Still's disease including nondefinite cases were collected from 32 institutions with rheumatology units in Japan. Each member of the committee carefully analyzed all of the patient report forms and independently gave the score indicating the degree of certainty of the disease to each patient. Then, based on the sum of the scores, 90 cases from 29 institutions were classified as definite cases by the committee. The remaining 56 cases (probable or possible cases) were excluded from further analysis.

The control diseases selected by the committee were those which might show similar features to adult Still's disease. With use of the same questionnaire as in the cases of adult Still's disease, data from the control patients were accumulated from 10 institutions where members of the committee were affiliated. The control group consisted of 267 individuals including 33 patients with sepsis, 31 with polyarteritis nodosa (PAN), 31 with seronegative rheumatoid arthritis (RA), 31 with polymyalgia rheumatica (PMR), 25 with rheumatoid vasculitis with various extraarticular features, 15 with Takayasu's arteritis, 11 with ankylosing spondylitis, 8 with psoriatic arthritis, 5 with arthritis associated with inflammatory bowel disease, 5 with Reiter's syndrome or other reactive arthritis, 5 with allergic purpura or hypersensitivity angiitis, 3 with Wegener's granulomatosis, 2 with temporal arteritis, 1 with allergic granulomatous angiitis, 1 with pustulotic arthroosteitis, and 62 with fever of unknown origin (FUO). All of these control diseases were diagnosed definitely at each institution. Concretely, sepsis was diagnosed by demonstrating a bacteremic state, and these patients had various original diseases, of which malignancies were the most numerous while rheumatic disease (rheumatoid arthritis) was seen in 2 patients. PAN and rheumatoid vasculitis with extraarticular features were diagnosed according to the diagnostic criteria prepared by the Japanese Ministry of Health and Welfare, which laid stress on histological confirmation of angiitis. Seronegative RA and PMR were diagnosed according to well accepted criteria[8,9]. Diagnosis of other control diseases was made according to clinical, laboratory, histological, and radiographic findings. Sixty-two cases of FUO were classified according to Petersdorf and Beeson's criteria[10], and some were finally diagnosed as infections (15 cases), malignancies (2 cases), allergic or rheumatic diseases (12 cases), and the other diseases (8 cases). No patient considered as adult Still's disease was included in the control group.

The statistical terms used and their definitions are as follows: sensitivity: probability of the test or procedure having positive result when the disease is present (=true positive rate); specificity: probability of the test or procedure having negative result when the disease is not present (= true negative rate); false positive rate: (1 − specificity); false negative rate: (1 − sensitivity); positive predictive value: probability that the disease is present when the test or procedure is positive; negative predictive value: probability that the disease is not present when the test or procedure is negative; likelihood ratio: true positive rate divided by false positive rate (= sensitivity / 1 − specificity); relative value: sensitivity(%) + specificity(%); accuracy: (true positives + true negatives) / (true and false positives + true and false negatives). For comparison of positive rate of each clinical feature between patients and controls, χ^2 test was used, and p value of over 5% was considered to be not significant.

Based on these statistical values calculated from the data on 90 cases of adult Still's disease and on 267 control cases, the most discriminating clinical items were listed. The list contained 8 items having 140 or greater relative value or about 90% or greater sensitivity. Then, various combinations of these items were applied to the patients and controls, and after sensitivity and specificity of each combination were evaluated, conditions required for a classification of adult Still's disease was determined.

According to Bayes' theorem[11], the disease prevalence and sensitivity and specificity of a test can determine the posttest probability (=predictive value) of having the disease in persons presenting positive test result. Therefore, using assumed prevalence of this disease in a population considered, and the sensitivity and specificity of different numbers of the satisfied criteria, the predictive value of adult Still's disease, which represented the clinical probability of this disease, was calculated.

RESULTS

Table 1 summarizes the sensitivity, specificity, relative value, and X²o-value of each clinical item. In all of the clinical features, typical rash had the highest relative value associated with relatively high sensitivity and almost complete specificity. Typical rash was defined by the committee as macular or maculopapular nonpruritic salmon-pink eruption usually appearing during fever. In the item of fever, various additional conditions as to the highest temperature and a febrile period, and their combined conditions were evaluated for those statistical values (data not shown). Also in the item of joint symptoms, various conditions concerning the duration of joint symptom, the number of affected joints and the presence or absence of arthritis, and their combined conditions were similarly evaluated (data not shown). Among these conditions, ''fever of 39°C or higher, lasting one week or longer'' and ''arthralgia lasting 2 weeks or longer'' showed the highest relative value (Table 1). In addition, the features of lymphadenopathy which were defined as recent development of significant lymph node swelling and of splenomegaly confirmed on palpation or by an echogram were combined into one item, ''lymphadenopathy and/or splenomegaly.'' This combination gave rise to higher sensitivity with little loss of the relative value (Table 1).

The statistical values of each laboratory finding are summarized in Table 2. In the items of hematological variables, erythrocyte sedimentation rate, and serum albumin level, several cutoff points were evaluated, and only those having the highest relative value were shown in this table. Among them, leukocytosis and granulocytosis, both of which were

Table 1. *Statistical values of clinical features*

	Sensitivity		Specificity		Relative	χ^2 Test	
	No.	%	No.	%	Value	χ^2o Value	
Female	60/90	67	116/267	43	110	2.8	NS
Age at onset 16–35 yrs	48/78*	62	169/250	68	130	21.2	p<0.001
Similar episode in childhood	11/89	12	250/260	96	108	8.5	p<0.005
Age at onset 16–35 yrs or similar episode in childhood	59/87	68	162/253	64	132	26.6	p<0.001
Fever	90/90	100	40/264	15	115	15.4	p<0.001
≥39°C and ≥ 1 week	63/83	76	191/251	76	152	72.5	p<0.001
Arthralgia	90/90	100	97/263	37	137	45.8	p<0.001
≥ 2 weeks	60/67	90	116/241	48	138	31.0	p<0.001
Arthritis	62/86	72	157/261	60	132	27.0	p<0.001
Typical rash	72/83	87	257/260	99	186	269.8	p<0.001
Weight loss (≥ 10%)	40/72	56	132/212	62	118	7.0	p<0.01
Sore throat	58/83	70	199/239	83	153	82.2	p<0.001
Lymphadenopathy	59/86	69	186/256	73	142	46.7	p<0.001
Splenomegaly	56/86	65	209/251	83	148	72.7	p<0.001
Lymphadenopathy and/or splenomegaly	73/87	84	153/247	62	146	54.1	p<0.001
Hepatomegaly	42/87	48	208/254	82	130	30.8	p<0.001
Pleuritis	11/89	12	218/259	84	96	0.6	NS
Pericarditis	9/87	10	234/248	94	104	2.2	NS
Pneumonitis	5/90	6	235/259	91	97	1.2	NS
Myalgia	50/89	56	167/261	64	120	11.1	p<0.001
Neurological involvement	11/89	12	193/263	73	85	7.6	p<0.01
Renal involvement	14/90	16	196/257	76	92	2.6	NS
Drug allergy/toxicity	44/82	54	197/252	78	132	30.0	p<0.001

The underlined features were those selected finally for the classification criteria by the committee.
* The patients with a similar episode in childhood were excluded.
NS: not significant.

Table 2. *Statistical values of laboratory findings*

	Sensitivity		Specificity		Relative	χ^2 Test	
	No.	%	No.	%	Value	χ^2o Value	
WBC ≥ 10,000/mm³	80/90	89	154/265	58	147	59.7	p<0.001
≥ 15,000/mm³	55/90	61	227/265	86	147	76.0	p<0.001
Granulocytes ≥ 80%	74/89	83	171/260	66	149	63.7	p<0.001
WBC ≥ 10,000/mm³ and granulocytes ≥ 80%	69/89	78	204/263	78	156	87.2	p<0.001
Hemoglobin < 10 g/dl	53/90	59	142/262	54	113	4.6	p<0.05
ESR ≥ 80 mm/h	69/89	78	114/247	46	124	15.3	p<0.001
Serum albumin < 3.5 g/dl	67/88	76	113/260	43	119	10.7	p<0.005
Liver dysfunction	74/87	85	155/263	59	144	50.7	p<0.001
Increased Ig level	66/87	76	91/233	39	115	6.2	p<0.025
Hypercomplementemia	60/89	67	119/216	55	122	12.8	p<0.001
Positive CIC	7/35	20	43/60	72	92	0.8	NS
Negative RF	84/89	94	64/233	27	121	18.3	p<0.001
Negative ANA	82/88	93	40/224	18	111	6.1	p<0.025
Negative RF and negative ANA	77/87	89	85/220	39	128	21.5	p<0.001
Negative result of blood culture	82/82	100	37/140	26	126	26.0	p<0.001
Negative PPD skin test	34/53	64	61/108	56	120	6.1	p<0.025
Hyperferritinemia	28/34	82	25/54	46	128	7.5	p<0.01
extremely increased*	20/30	67	44/52	85	152	22.2	p<0.001

The underlined features were those selected finally for the classification criteria by the committee.
* 4-times as high as normal upper limit or higher.
WBC: white blood cell, ESR: erythrocyte sedimentation rate, Ig: immunoglobulin, CIC: circulating immune complexes, RF: rheumatoid factor, ANA: antinuclear antibody, PPD: purified protein derivative, NS: not significant.

the important features having high relative value, were represented by a combined item of "10,000/mm³ or more of white blood cell (WBC) counts including 80% or more of granulocytes," resulting in higher relative value. In the item of liver dysfunction, the abnormality of individual hepatic enzyme tests and their combined conditions were evaluated (data not shown). The representative item showing the highest relative value was an abnormally elevated level of transaminases and/or lactate dehydrogenase, which was attributed to liver damage associated with this disease but not with drug allergy/toxicity or other causes. Serum ferritin level seemed to be a useful discriminating factor of this disease from the control diseases (Table 2). However, since the number of analyzed patients and controls was considerably small compared with that in the other features, we could not include this feature in further analysis.

As items required for a construction of classification criteria, the committee selected features having high relative value from those listed in Table 1 and Table 2. The clinical features with 140 or greater relative value were as follows: "typical rash," "10,000/mm³ or more of WBC and 80% or more of granulocytes," "39°C or higher of fever lasting one week or longer," "sore throat," "lymphadenopathy and/or splenomegaly," and "liver dysfunction." In addition, the committee considered another 2 features to be included in the criteria list, because they had very high sensitivity and are important for making an outline of the disease. One was the joint symptom, and its representative item was "arthralgia lasting 2 weeks or longer." The other additional feature was the combined item, "negative rheumatoid factor and negative antinuclear antibody." The specificity of this feature was relatively low, because most of the control diseases analyzed were seronegative for autoantibodies. However, in the actual differential diagnosis of this disease, the presence or absence of these autoantibodies seemed to be one of the critical factors.

Consequently, the items selected by the committee consisted of 8 clinical items. Then, these 8 criteria were applied to 53 patients with definite adult Still's disease and 164 control patients whose histories were available for all of the criteria. Table 3 shows the representative results of the performance of 8 criteria in various conditions. When all criteria were given equal weight, the condition meeting 5 or more criteria revealed the highest relative value. As a next trial, the committee divided them into 4 major and 4 minor ones. The major criteria having very high sensitivity or high relative value were fever, arthralgia, typical rash, and leukocytosis. The minor criteria were the remaining 4 features. In this setting, the condition meeting 5 or more criteria including 2 or more major criteria yielded the highest relative value.

Considering the performance of the selected items in various conditions, the committee proposed the preliminary criteria for a classification of adult Still's disease as shown in Table 4. The classification of this disease requires a total of 5 or more of the criteria including 2 or more of the major criteria. This condition gave rise to 96.2% sensitivity and 92.1% specificity. However, 13 control cases satisfied the proposed criteria. They were 2 cases of PAN, 2 cases of rheumatoid vasculitis with extraarticular features, 1 case of sepsis and 8 cases of FUO, and the final diagnosis of 8 FUO cases were probable viral meningitis, human immunodefi-

Table 3. *Comparative performance of the proposed criteria in various conditions*

Conditions in Applying 8 Proposed Criteria	Sensitivity (%)	Specificity (%)	Relative Value
When given equal weight*			
4 or more criteria	100.0	75.0	175.0
5 or more criteria	96.2	89.6	185.8
6 or more criteria	83.0	98.2	181.2
When divided into 4 major and 4 minor†			
Major 2 or more & minor 2 or more	98.1	85.4	183.5
Total 4 or more (major 2 or more)	100.0	84.1	184.1
Total 5 or more (major 2 or more)	96.2	92.1	188.3

The 8 selected criteria were applied to 53 patients with definite adult Still's disease and 164 control patients, and the performance of the criteria in various conditions were evaluated (for details, see text). Only the representative results were shown.

* On the condition that 8 criteria were given equal weight.

† On the condition that 8 criteria were divided into 4 major and 4 minor (for details, see text and Table 4).

Table 4. *Preliminary criteria for a classification of adult Still's disease*

Major criteria
1. Fever of 39°C or higher, lasting 1 week or longer
2. Arthralgia lasting 2 weeks or longer
3. Typical rash*
4. Leukocytosis (10,000/mm³ or greater) including 80% more of granulocytes

Minor criteria
1. Sore throat
2. Lymphadenopathy and/or splenomegaly†
3. Liver dysfunction‡
4. Negative RF and negative ANA¶

Exclusions
I. Infections (especially, sepsis and infectious mononucleosis)
II. Malignancies (especially, malignant lymphoma)
III. Rheumatic diseases (especially, polyarteritis nodosa and rheumatoid vasculitis with extraarticular features)

Classification of adult Still's disease requires 5 or more criteria including 2 or more major criteria§.
Any disease listed under "Exclusions" should be excluded.

* Macular or maculopapular nonpruritic salmon-pink eruption usually appearing during fever.

† Lymphadenopathy is defined as recent development of significant lymph node swelling, and splenomegaly is confirmed on palpation or by an echogram.

‡ Liver dysfunction is defined as an abnormally elevated level of transaminases and/or lactate dehydrogenase, which is attributed to liver damage associated with this disease but not with drug allergy/toxicity or other causes. For the differentiation, it is recommended to see if liver function returns to normal upon discontinuation of hepatotoxic drug or not, before applying this criterion.

¶ RF in serum must be negative by routine test for the detection of IgM RF, and serum ANA must be negative by routine immunofluorescence test.

§ All criteria are applicable only in absence of other clinical explanations.

RF: rheumatoid factor, ANA: antinuclear antibody.

ciency virus associated complex, Takayasu's arteritis complicated with sepsis, hypersensitivity angiitis, and sarcoidosis in one case each, and unknown in 3 cases. To avoid the overdiagnosis, the committee set up the exclusions such as infections, malignancies, and rheumatic diseases (Table 4).

In addition, the present criteria were compared with various existing sets of diagnostic criteria of adult Still's disease. These sets of criteria were applied to our samples, but exclusions were not considered in application to the control cases. Table 5 shows the sensitivity, specificity, relative value, likelihood ratio, and accuracy of existing sets of criteria in comparison with our criteria. Our criteria showed much better sensitivity with a little loss of specificity, resulting in the greatest relative value as well as the best accuracy. However, as for the likelihood ratio, our criteria performed the least well because of its specificity (92.1%). The likelihood ratio depends on specificity much more than sensitivity, and indeed those with the highest likelihood ratio showed only 51% sensitivity. When applied to 194 non-Japanese cases collected from the literature[2], our criteria revealed nearly 100% sensitivity.

A numerical approximation of the clinical probability can

Table 5. *Comparative performance of various sets of criteria for adult Still's disease*

Set	Sensitivity (%)	Specificity (%)	Relative Value	Likelihood Ratio	Accuracy (%)
Goldman, *et al*[3]	44.7	98.9	143.6	39.4	86.8
Calabro & Londino[4]	60.9	98.1	159.0	31.6	88.7
Reginato, *et al*[5]	51.2	99.2	150.4	67.9	87.9
Cush, *et al*[6]	80.0	96.9	176.9	26.0	92.8
Present criteria	96.2 (99.3)*	92.1	188.3	12.1	93.1

Various existing sets of diagnostic criteria were applied to 90 definite cases of adult Still's disease and 267 control cases collected in our study.

* When applied to 194 non-Japanese cases collected from the literature[2].

study and the prevalence of this disease. Although a precise prevalence of adult Still's disease is unknown at present, in one of our rheumatology clinics the patients with this disease have been 2.9% of the total patients (unpublished observation), and Bujak, *et al* have found that 5% of the patients with FUO had this disease[12]. Using the latter value (5% in FUO group), and the sensitivity and specificity of different numbers of the proposed criteria, the predictive value (the clinical probability) of increasing numbers of satisfied criteria was calculated (Figure 1). For convenience, this calculation was performed on the condition that all criteria were given equal weight. In this figure, for example, it is recognized that a patient with FUO satisfying 5 of the proposed criteria would have a 33% chance of having adult Still's disease. However, on the proposed condition that 5 or more of the criteria including 2 or more of the major criteria are needed for a classification, specificity increased from 89.6% to 92.1% (Table 3) while sensitivity remained unchanged. Therefore, when these figures (96.2% sensitivity, 92.1% specificity, and 5% prevalence) were applied to Bayes' formula, the predictive value became 39%.

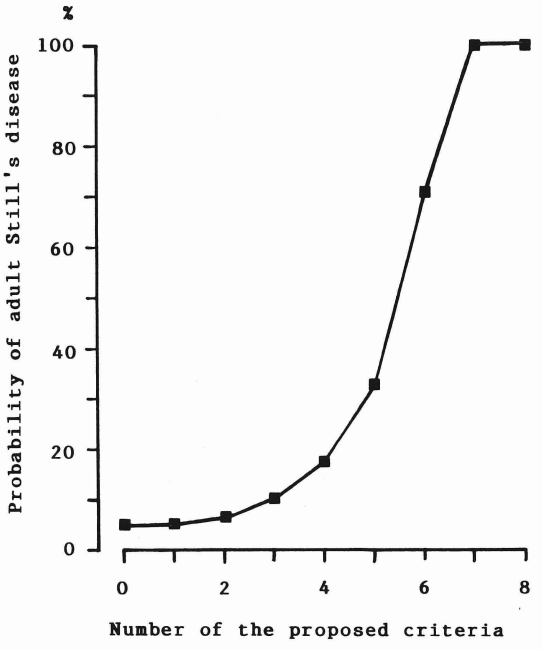

Fig. 1. Probability of adult Still's disease with varying numbers of the proposed criteria. For details, see text.

DISCUSSION

The clinical manifestations of adult Still's disease consist of miscellaneous nonspecific features[2,7]. Moreover, some patients may not present all of the characteristic features such as high fever, joint symptoms, rash, and leukocytosis, especially at an early stage of illness. Delay in recognition of the disease may result in prolonged and unnecessary investigations or in unwarranted therapy. Previously, there have been no diagnostic or classification criteria of this disease that were established through a statistical process. In our study, we compared the various features in 90 cases of adult Still's disease with those in 267 control cases, both of which were collected from multiple institutions with rheumatology units in Japan. The cases of adult Still's disease were those considered to be a definite group by the committee as reported[7], and probably this might increase the sensitivity of each criterion. Since selection of the control diseases was critical in evaluating the specificity, the committee, after due consideration, selected those which were confusing with this disease, such as seronegative arthritis, various forms of vasculitis, sepsis, and FUO, as a control group.

Out of a number of potential disease discriminators and their combinations, 6 items having high relative value (140 or greater) and an additional 2 items having very high sensitivity were selected by the committee as the most discriminating features. There were 2 opinions in the committee concerning whether all criteria should be given equal weight or some should be given greater weight. Equal weighing can be used more simply, but there may be a possible overdiagnosis in a point scoring patient with accumulation of less characteristic (minor) features. The committee preferred the view that some features which characterized this disease more impressively should be separated from the others. So, 4 features having very high sensitivity or high relative value, such as fever, arthralgia, typical rash, and leukocytosis, were classified as major criteria and the remaining 4 features were classified as minor criteria. In fact, this classification yielded higher specificity with no loss of sensitivity than when given equal weight.

The articular lesions should be seriously considered in this disease as reported recently[13]. Our criteria included as a major manifestation ''arthralgia lasting 2 weeks or longer'' which was the representative item showing the highest relative value among those concerning joint symptoms, despite its relatively low specificity. When ''arthritis'' was substituted for ''arthralgia'', sensitivity was considerably decreased. However, the definition of this criterion may need further refinement.

Although usually, the greater the sensitivity of a feature, the lower its specificity, and vice versa, an exception in this disease is typical rash which has nearly 100% specificity and relatively high sensitivity. In addition to the committee's original definition, the rash typical of this disease was considered to have the following characteristics: distribution is not diffuse or over the whole body but localized mostly on trunk and proximal extremities; the form of eruption varies from place to place even in the same patient; scattered small eruptions and their coalescent forms are seen at the same time; and rash can be produced readily by thermal or mechanical stimulation (positive Köbner's phenomenon). Because of these characteristics, it must be noted that typical rash of this disease can be overlooked without careful observation.

Since the patients with this disease tend to develop liver dysfunction attributed to hepatotoxic drugs such as antibiotics and nonsteroidal antiinflammatory drugs[7], the sensitivity of liver dysfunction may be overestimated, although the questionnaire for the survey had included the proviso that liver dysfunction apparently attributable to such drugs should be excluded. When applying the proposed criteria to a patient having liver dysfunction, particular attention should be paid.

Unfortunately, we could not include ''increased level of serum ferritin'' in the criteria list, because of insufficient data available compared with that of other features. However, even our incomplete data showed that this feature could be an important discriminator[2]. The future revision of the criteria will determine the inclusion of this feature.

When the existing 4 sets of criteria[3-6] were applied to our samples, all showed an excellent specificity, but sensitivity was extremely low in most, contrary to our criteria giving much greater sensitivity with a little loss of specificity. However, a comparison of likelihood ratios showed that our criteria performed the least well, since likelihood ratio was greatly decreased by a small loss of specificity. Generally, the classification criteria having higher sensitivity with lower specificity are suitable for screening the patients, although there may be a risk of overdiagnosis. On the other hand, those having higher specificity with lower sensitivity are suitable for a definite diagnosis, though these criteria may need months or years to be satisfied and false-negative patients may increase. In order to reduce the patient's chance of having unnecessary diagnostic procedures or unwarranted therapy, it is important to recognize the disease as early as possible, avoiding overdiagnosis. From this viewpoint, the balance of sensitivity (96.2%) and specificity (92.1%) of our criteria seems reasonable. However, since overdiagnosis of this disease may be dangerous, an exclusion process for diagnosis will be necessary. In fact, of 13 false-positive patients in our study, 7 patients with connective tissue diseases or associated disease and 3 cases of infections can be eliminated by careful exclusion process, and this will raise the specificity to 98.2%.

According to Bayes' theorem[11], we have calculated the probability that a patient with FUO has adult Still's disease when a patient satisfies the present criteria. It was found that despite relatively high sensitivity and specificity of the criteria, the probability was only 39%. This seemingly poor performance is due to the strong dependence of Bayes' theorem on the prevalence of a disease in a certain population. In a similar study of the patients with systemic lupus erythematosus[14], when the prevalence was 0.14%, a chance of having lupus in a patient meeting 1971 American Rheumatism Association criteria was reported to be only 5%, but if the prevalence was 10%, the probability would increase up to 79%. Figure 2 shows a change of the predictive values calculated from sensitivity (96.2%) and specificity (92.1%) of our criteria using Bayes' theorem in varying rates of prevalence. In this figure, positive predictive value means the probability that adult Still's disease is present when the present criteria are satisfied, and negative predictive value means the probability that the disease is not present when the criteria are not satisfied. As shown in the figure, when our criteria are applied to the patients with low pretest probability (prevalence), the posttest probability (positive predictive value) is not so high. When the prevalence becomes 40%

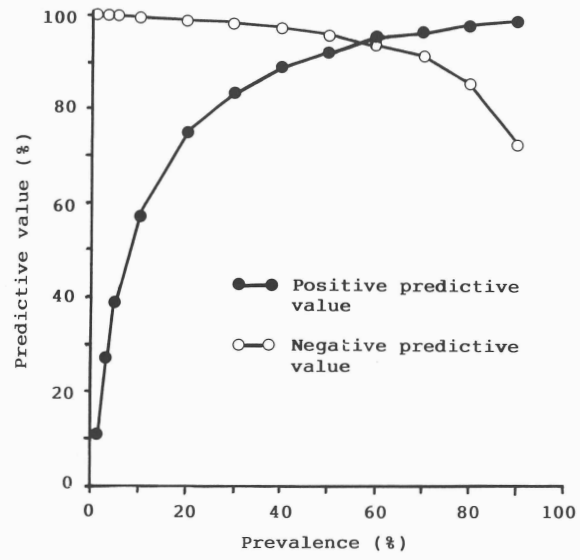

Fig. 2. Predictive values of adult Still's disease in a patient satisfying the proposed criteria in varying rates of the disease prevalence. For details, see text.

or higher, the probability of having this disease in a patient satisfying the criteria increases to 90% or higher. It means that before applying the criteria the selection of the patients by means of careful history taking and close examination will greatly increase the accurate classification and considerably reduce the false-positives. In practice, an exclusion process will play a role in this selection. In addition, Figure 2 shows that our criteria had a very good function for excluding this disease, because the predictive value of negative result is very high. However, when the prevalence is extremely high, negative predictive value falls down somewhat, and the percentage of false-negative patients will increase.

In our study, all of the patients were Japanese. As reported[7], the incidence of each clinical manifestation in these 90 cases was almost the same as in 194 non-Japanese cases of adult Still's disease collected from the literature except for some features: A female preponderance, weight loss, splenomegaly, liver dysfunction, and hypercomplementemia had a higher incidence in Japanese, and young onset (16-35 years old), high fever ($\geq 39°C$), pleuritis, and pericarditis a lower incidence in Japanese cases. Among these features, those included in our criteria are splenomegaly, liver dysfunction, and high fever. Though the incidence of high fever is higher in non-Japanese than in Japanese cases and the other 2 features, splenomegaly and liver dysfunction, are included in the minor criteria, there may be some problems in the application of our criteria to non-Japanese patients. As a matter of fact, however, our criteria showed very high sensitivity (99.3%) when applied to 194 non-Japanese cases collected from the literature[2], though specificity for the non-Japanese patients remained unknown. Further appropriate validation will be required by a wide application to patients and controls and also prospectively to a new group of the patients with this disease. This is the first attempt to prepare the classification criteria of adult Still's disease by the proper proceedings, and it is anticipated that the proposed criteria will require some modifications to improve their usefulness.

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