A Four Year Follow-Up of Suspected Rheumatoid Arthritis: The Tecumseh, Michigan, Community Health Study

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Of 563 individuals suspected of having rheumatoid arthritis when examined in 1959-1960, only 402, or 71.4 per cent, participated in the Tecumseh, Michigan, Community Health Study of 1962-1965. Of the 402, when classified by similar criteria, only 107, or 26.6 per cent, maintained their former classification as to degree of certainty of presence of rheumatoid arthritis, while 200, or 49.8 per cent, showed no evidence of the disease. The results illustrate some of the difficulties and uncertainties of prospective studies.

IN THE Tecumseh Community Health Study in 1959-1960, approximately 90 per cent of the residents of Tecumseh, Michigan, underwent a comprehensive health examination (TCHS I) in the course of which information was collected regarding certain symptoms, physical findings, and laboratory manifestations of rheumatic diseases. Similar information was collected during a second series of examinations in 1962-1965 (TCHS II). This report represents a follow-up of the 563 respondents who in 1959-1960 had clinical findings suspicious for rheumatoid arthritis or a positive latex fixation test for rheumatoid factor.

METHODS

The methods employed in the first series of examinations have been reported.[1] During the second round of examinations, conducted during 1962-1965, the examination procedures were very similar except that several additional methods were included. To the latex fixation tube dilution test[2] which was employed in TCHS I, a commercial slide latex fixation test[3] and a human erythrocyte agglutination test (HEAT)[4] were added as serologic tests for rheumatoid factor. In addition, in TCHS II it was possible to obtain roentgenograms of the hands and wrists (anteroposterior view) and of the cervical spine (lateral view in flexion), of the majority of participants 20 years of age or over.

The tube dilution latex fixation test was considered positive if flocculation occurred in a dilution of 1:20 or greater. The slide modification was considered positive if the result was "reactive" as defined by the manufacturer; weakly reactive results were not considered significant. In the case of the human erythrocyte agglutination test, agglutination in a dilution of 1:16 or greater was regarded as positive.

The radiographs of the hands and wrists and cervical spine were interpreted by the authors using the Atlas of Standard Radiographs of Arthritis as a reference guide.[5]

Inso far as possible the American Rheumatism Association (ARA) diagnostic criteria for rheumatoid arthritis[6] were used as the basis of diagnostic classification in TCHS I. Only 7 of the 11 criteria could be applied since radiologic examination of the joints was not made, nor was it feasible to examine synovial fluid or the histologic features of the synovialis or subcutaneous nodules. The fol-

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lowing four degrees of diagnostic certainty were employed:

1. Questionable: These individuals had only joint pain or tenderness or morning stiffness, or a history of joint swelling; thus they failed to meet the criteria for any of the defined diagnostic categories.

2. Possible: The ARA criteria were employed, except that sedimentation rates and C-reactive protein tests were not performed.

3. Probable: These subjects fulfilled three or four of the ARA diagnostic criteria.

4. Likely: These subjects fulfilled five or more of the A.R.A. diagnostic criteria; this group therefore also includes those few individuals with "classical" rheumatoid arthritis.

The comparability of the diagnostic classifications in TCHS II was complicated by the addition of radiologic examinations, so that information was obtained regarding 8 of the 11 criteria. The classification scheme was somewhat modified and simplified from TCHS I, as follows:

1. Possible cases: One or two of the ARA diagnostic criteria present; this group is therefore comparable to the questionable and possible categories of TCHS I.

2. Probable: Three or four of the criteria present.

3. Likely: Five or more of the criteria present; this group therefore includes "definite" and "classical" cases as defined by the ARA criteria.

This scheme offers advantages for purposes of comparison with earlier population studies, which generally have reported only the number of probable and definite cases.

Results

Following completion of the second series of examinations, it was found that 402, or 71.4 per cent, of the 563 individuals with clinical suspicion of rheumatoid arthritis and/or a positive latex fixation test in TCHS I had been reexamined. This represents a rate of loss of 28.6 per cent between the two examination periods. The interval between examinations was highly variable inasmuch as the method of calling in participants was changed in TCHS II; the average interval was approximately 4 years, and approximately 98 per cent of subjects were examined within 3 to 6 years.

Comparison of those subjects who participated only in TCHS I with those who participated both in TCHS I and II indicated that the two groups did not differ to a statistically significant degree with respect to most of the characteristics in which they could be compared. They were alike as to distribution by age, sex, type of arthritis, degree of certainty of diagnosis of rheumatoid arthritis, distribution of latex fixation test titers, and distribution within the samples and strata of the total population. Thus, for all practical purposes, the loss of 28.6 per cent of individuals of interest over an average period of 4 years did not change in any major way the group characteristics of those who could be followed through a second examination.

The diagnostic status of these 402 respondents is indicated in Table 1. It will be observed that on reexamination 200 (49.8 per cent) had no evidence of rheumatoid arthritis, while 63 (16.9 per cent) were in the possible category, 29 (7.2 per cent) in the probable category, 8 (1.9 per cent) in the likely category, and 97 (24.1 per cent) had one or more positive rheumatoid factor tests as their only abnormality. Of the total 402, only 107 (26.6 per cent) remained in the same diagnostic category as a result of both examinations.

It is of interest to consider the changes in diagnostic classification between TCHS I and II in greater detail. Of the 231 subjects who were classified as questionable or possible cases of rheumatoid arthritis in TCHS I, only 15 (6.5 per cent) had become probable and only one (0.4 per cent) had become likely in TCHS II; 48 (20.8 per cent) remained in the possible category, 39 (16.9 per cent) had only a positive serologic test for rheumatoid factor, while 128 (55.4 per cent) had no evidence whatsoever of rheumatoid arthritis. Of the 47 persons originally classified as probable cases, 6 (12.8 per cent) remained in that category, while 3 (6.4 per cent) became

Table 1.—Changes in the Distribution of the Degree of Certainty of Diagnosis of Rheumatoid Arthritis in 402 Persons over an Average of Four Years' Time, TCHS 1959–1960 to 1962–1965

Certainty of diagnosis in 1959–1960	Total reexamined, 1962–1965	Certainty of diagnosis in 1962–1965 examinations				
		No evidence of disease	Questionable or possible	Probable	Likely	Positive L.F.* test only
Questionable or possible	231	128 (55.4)†	48 (20.8)	15 (6.5)	1 (0.4)	39 (16.9)
Probable	47	22 (46.8)	10 (21.3)	6 (12.8)	3 (6.4)	6 (12.8)
Likely	19	4 (21.0)	2 (10.5)	6 (31.6)	4 (21.0)	3 (15.8)
Positive L.F. test only	105	46 (43.8)	8 (7.6)	2 (1.9)	0 (0.0)	49 (46.7)
Total	402	200 (49.8)	68 (16.9)	29 (7.2)	8 (2.0)	97 (24.1)

* One or more of the following tests: slide latex fixation test; tube dilution latex fixation test or human erythrocyte agglutination test.

† Per cent relation of the number to the row total.

likely cases; 10 (21.3 per cent) dropped back into the possible category, 6 (12.8 per cent) had only a positive rheumatoid factor test, and 22 (46.8 per cent) had no evidence of rheumatoid arthritis. Subjects who were originally in the likely group showed the least change, but even here only 4 (21 per cent) were unchanged in TCHS II; 6 (31.6 per cent) were reclassified as probable, 2 (10.5 per cent) as possible, 3 (15.8 per cent) had only a positive rheumatoid factor test, and 4 (21 per cent) had no evidence of rheumatoid arthritis. Of the 105 respondents who had a positive latex fixation test as the only evidence of rheumatoid arthritis in TCHS I, none was found to have likely disease on reexamination and only 2 (1.9 per cent) probable and 8 (7.6 per cent) possible rheumatoid arthritis; 49 (46.7 per cent) continued to have a positive serologic test for rheumatoid factor as their only abnormality, and 46 (43.8 per cent) had no evidence of rheumatoid arthritis. Those subjects whose tests became negative were observed for the same average length of time, 4.1 years, as were those whose tests remained positive. Of those subjects with initially high titers (1:640 or greater), 43 per cent remained positive after an average of 4.4 years while those with initially low titers (1:20–1:320 inclusive) had corresponding values of 45 per cent and 3.7 years. Of these 105 subjects, only 25 (23.8 per cent) were positive by the same latex fixation tube dilution technic in both studies.

Discussion

These results illustrate the difficulties and uncertainties of prospective studies of rheumatoid arthritis and serologic tests for rheumatoid factor. In part, the difficulty arises from the fact that rheumatoid arthritis pursues a fluctuating course with at least partial remissions and exacerbations. In some cases transient episodes of disease may occur which do not leave permanent evidences of deformity and which may be easily forgotten by the patient in a 4 year period. While most population studies suggest a much broader spectrum of severity of rheumatoid arthritis than do hospital- or clinic-based studies, there is still uncertainty about the minimal requirements for a diagnosis. It seems probable that a number of nonrheumatoid musculoskeletal conditions, such as posttraumatic joint disease and postviral arthritis, confuse the results

of population studies by fulfilling the diagnostic criteria for rheumatoid arthritis to varying degrees. It may be impossible to separate these nonrheumatoid conditions from rheumatoid arthritis in a single examination or to differentiate them from remittent and/or intermittent rheumatoid arthritis on repeated examination. It seems unlikely that this dilemma will be resolved until an etiologic definition of rheumatoid arthritis is at hand.

The nonspecificity of rheumatoid factor tests is well recognized, as is the fact that they may be present transiently during or following various infectious diseases, including subacute bacterial endocarditis, syphilis, yaws, leprosy, tuberculosis, infectious hepatitis, kala azar, and schistosomiasis.[7] The situation has been compared to that previously observed with the serologic tests for syphilis, where acute or chronic false positive results may occur. Considerable interest has centered on the possibility that positive tests for rheumatoid factor may select individuals with an increased risk of subsequent development of clinical rheumatoid arthritis. The very limited data available at present regarding this possibility are conflicting and do not provide a clear answer. Ball and Lawrence,[8] on reexamining after 5 years 19 seropositive subjects who originally had no accompanying clinical or radiological evidence of rheumatoid arthritis, found that 7 had developed evidence of the disease, as compared to only 5 of 57 seronegative subjects similarly followed. In a similar study, Finnish investigators[9] found that after an interval of 9 years none of a small group of 7 subjects with apparently false-positive sheep cell agglutination tests on original examination had developed rheumatoid arthritis and that 4 had become seronegative. More recently, 3 apparently normal individuals with high titers of rheumatoid factor were reported not to have developed rheumatoid arthritis after an interval of 6 to 9 years, although the first had experienced arthralgias and a nonspecific conjunctivitis, the second intermittent eye symptoms, and the third an episode of polyarthralgia followed later by a "tennis elbow."[10] In a brief communication,[11] this third patient is subsequently reported to have developed clinical and laboratory evidence of probable systemic lupus erythematosus. In the Tecumseh community, it was found that only about 24 per cent of otherwise healthy seropositive respondents remained seropositive by the same technic after an average interval of 4 years. Of this group of originally seropositive subjects, none was found to have developed definite or classic rheumatoid arthritis in this average 4 year follow-up period, and only 1.9 per cent were found to have evidence for probable and 7.6 per cent evidence for possible disease.

Similarly, there seemed to be little evidence that the varying diagnostic categories of rheumatoid arthritis constituted a gradient along which respondents progressed toward a more certain diagnosis, although the correlation coefficient (r) of Table 1 is 0.401. In fact, of those respondents originally in the possible and probable categories, the great majority moved downward in the diagnostic scale and about half were found to have *no* evidence of rheumatoid arthritis. Even in the group originally classified as having definite rheumatoid arthritis this trend was apparent, with 21 per cent showing no evidence of disease on reexamination. Again, these findings are compatible either with the view that rheumatoid arthritis, as it occurs in the general population, pursues a much more variable course than observed in hos-

pital or clinic settings, or with the view that the picture is obscured by a number of nonrheumatoid arthropathies which are more frequently transient or self-limited. It seems likely that both factors contribute to the observed results.

SUMMARIO IN INTERLINGUA

Inter 563 individuos con suspicion de arthritis rheumatoide quando illes esseva examinate in 1959/60, solo 402 (o 71,4 pro cento) participava in le Studio de Hygiene Communal de Tecumseh, Michigan, de 1962 ad 1965. Quando le 402 esseva classificate a base de simile criterios, solo 107 (26,6 pro cento) manteneva lor previe classification con respecto al certitude del presentia de arthritis rheumatoide, durante que 200 (49,8 pro cento) monstrava nulle evidentia del morbo. Le resultatos illustra certes del difficultates e incertitudes in studios prospective.

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