

Early rheumatoid disease

I. Onset

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Fleming, A., Crown, J. M., and Corbett, M. (1976). *Annals of the Rheumatic Diseases*, **35**, 357–360. **Early rheumatoid disease. I. Onset.** We describe features with onset in 102 patients seen within the first year of rheumatoid disease. The male:female ratio was approximately 3:4, suggesting a near equal sex incidence at onset. The disease started more often in the colder months and was usually insidious, symmetrical, and involved the upper limbs.

The patients were followed prospectively and outcome was assessed after a mean of 4·5 years. Older patients fared worse and there was a trend for a poorer prognosis to be indicated by an insidious onset and early progression to symmetrical involvement.

The importance of observing all phenomena associated with onset in a condition such as rheumatoid disease, where cause and cure are unknown, has been stressed by Jacoby, Jayson, and Cosh (1973). Studies attempting this rely on patient memory, and a defect of many such works has been the length of time after which patients have been asked to recall early episodes. It is difficult to find and follow rheumatoid sufferers early in the course of their disease, and as a result only a few reports are based on data obtained near the onset of joint symptoms (Otten and Boerma, 1959; Rotes-Querol and Roig-Escofet, 1968; Jacoby and others, 1973).

A recent prospective study of early rheumatoid disease, undertaken at the Middlesex Hospital, has provided information on various aspects of onset, including age, sex, time, type, site, symmetry, and time-lag to presentation, enabling the significance of these data to be assessed in relation to other disease features and to subsequent course. The information was taken at a mean 4·6 months from onset, when patient memory was relatively fresh.

Patients and methods

Patients were invited to enter the study if the rheumatologist suspected rheumatoid disease of less than one year's duration. Those with evidence of psoriatic arthritis, gout, ankylosing spondylitis, Reiter's disease, or colitic arthropathy were excluded. At this first specialist

rheumatological consultation the historical data on onset was gathered. The patient subsequently attended a special research clinic three times a year.

At the special clinic the site of involvement (swelling, tenderness, or pain on movement) was noted, the rheumatoid status was recorded (American Rheumatism Association, 1959), and the patient was placed in one of four functional grades (Duthie and others, 1955). Annual radiographs were taken of hands, feet, and cervical spine, and the presence of erosions was recorded. The sheep cell agglutination test (SCAT) was used to estimate rheumatoid factor (Roitt and Doniach, 1969). The clinics were quite distinct from the regular outpatient visits and treatment was not influenced.

One hundred and two patients were studied, and were followed in the clinic for 18 months or longer, or until death. The mean delay from onset to the first specialist consultation and to the first research clinic visit was respectively 4·6 months and 7·9 months. Mean disease duration was 4·5 years.

At the first clinic visit, 41 (40·6%) were SCAT positive, 25 (24·5%) were erosive, 48 (47·1%) were in functional grade II or worse, and 70 (68·6%) were either 'definite' or 'classical'. With the passage of time 67 (66%) became seropositive at some stage and 70 (68·6%) became erosive.

Twenty-two patients who could have satisfied the time criteria for inclusion in the analysis were lost to the study, including 18 females (23·7% of eligible females) and 5 males (10·2% of eligible males). 9 of these can be accounted for, but in 13 the reason is unknown. All are still alive. Thus, proportionally more men continued as attenders. The mean age of defaulters is higher (7·5 years

Table I *Month of onset*

<i>Month</i>	<i>J</i>	<i>F</i>	<i>M</i>	<i>A</i>	<i>M</i>	<i>J</i>	<i>J</i>	<i>A</i>	<i>S</i>	<i>O</i>	<i>N</i>	<i>D</i>
No. of onsets	10	12	8	7	8	4	6	4	8	9	13	12

older for males, 2.7 for females). There are no further significant differences between the defaulters and those who remained in the study in other measurements at the first clinic visit, including ARA criteria, functional grade, and serology.

The patients were divided into three prognostic groups according to the overall course the disease had taken. The clinical features on which this is based are non-laboratory and reflect pain and incapacity. An improved group contains patients who have improved to, or remain in, functional grade I, and who have minimal or no residual problems as measured by joint involvement, early morning stiffness, or grip strength. Those in a second group have improved to, or remained in, functional grade I, but still suffer mildly from some joint involvement, early morning stiffness, or loss of grip strength. A third group contains those who have been more severe or deteriorating. These have been persistently in functional grade II or worse, or have suffered persistently as measured by joint involvement, early morning stiffness, and grip strength. 26 patients improved, 14 pursued a mild steady course, and 62 a persistently more severe or deteriorating course.

Time of onset was considered as the first appearance of joint symptoms. Type of onset was based on both rapidity and severity of development of joint problems along the lines of Short, Bauer, and Reynolds (1957). However, unlike them, we found it necessary to subdivide this variable into three groups: *sudden*, where onset of severe joint problems could be isolated to an hour or a day; *intermediate*, where this could be isolated to days or weeks; and *slow*, where it could be isolated to weeks or months. Symmetry was considered to be present if there was bilateral involvement of corresponding joints.

The data were transferred to 80-column punch cards for subsequent computer analysis using the facilities of the Manchester Regional Computer Centre.

Results

The group included 44 males and 58 females. Mean age at onset was 49.2 years (males 49.1, females 51.8) range 19–74 years. The peak age incidence for both sexes was in the 55- to 64-year age group. Age was related to outcome ($r=0.228$; $P<0.05$) with the older age groups having a more severe disease.

MONTH OF ONSET

Almost twice as many patients first developed joint problems during the winter months. 64 (62.7%) began in the months of October to March inclusive, and 37 (36.3%) began in the other months. November, December, and February showed the highest incidences (Table I). Information is missing in one case.

TYPE OF ONSET

A slow onset was seen in 69 patients (68.3%), 18 (17.8%) had an intermediate type, and 11 (10.9%) a sudden onset. A further 3 had an onset typical of palindromic rheumatism. Information is missing in one case. A slow onset correlated with the early presence of erosions ($P<0.05$), with 22 of the 25 who were erosive at the first clinic visit having a slow onset. Only 2 who were in the intermediate or sudden onset groups showed early erosions. There was also a strong trend ($r=0.192$; $P=0.055$) for the type of onset to have prognostic significance. A sudden onset was associated with a milder outcome, and a slow onset with a more severe outcome.

TIME FROM ONSET TO PRESENTATION

Time from onset of joint symptoms to the first specialist rheumatological consultation was 4.6 months. Information is missing in one case. 43 patients presented in the first 3 months, including 16 males and 27 females. Males did not present earlier than females.

SITE OF ONSET

Multiple joint involvement (29%), followed by hand involvement (28%), were the most common sites of onset (Table II). More broadly viewed, 56% had initial involvement of the upper limbs, 28% of the lower limbs, while 15% had both. Information is missing in 2 cases. The group with feet first affected developed erosions earlier ($P<0.01$) and they were more severe in the first year as measured by the number of ARA criteria present ($P<0.05$).

Table II *Site of onset*

<i>Joint involved</i>	<i>Frequency (%)</i>
Hand	28
Wrist	8
Elbow	3
Shoulder	4
Foot	13
Ankle	6
Knee	8
Spine	1
Multiple	29

SYMMETRY AT ONSET

Symmetrical joint involvement at onset was seen in 71 (70.3%) and asymmetry in 29 (28.7%). One

patient had initial spinal pain, and information is missing in one case. Symmetry or otherwise did not correlate with other variables.

SUBSEQUENT SYMMETRY

The arthritis became symmetrical within one year in 87 (85.3%) patients. This was associated with a more severe disease state as measured by the number of ARA criteria ($P < 0.01$) and the functional grade ($P < 0.05$). A strong trend was also noted for symmetry of involvement within the first year to indicate a worse outcome ($r = 0.1877$; $P = 0.059$).

Discussion

The sex ratio seen here of approximately 4 females to 3 males conflicts with much of the literature where the ratio tends to vary from about 2 to 1 to 4 to 1 (Garrod, 1890; Jones, 1909; Sclater, 1943). Even if the defaulters are included, the ratio of females to males in this study is 3 to 2. A proportion of 64% females was remarkably consistent in the studies of the Empire Rheumatism Council (1959), Short and others (1957), and Jacoby and others (1973); while Duthie and others (1955) had 72.7% females in their study. Most of these studies, however, dealt with patients accepted at variable times after onset. Two studies which have dealt exclusively with the early stages of rheumatoid arthritis are of special interest, that of Jacoby and others (1973) and of Otten and Boerma (1959). Both reported on the sex composition in the groups presenting within 3 months of onset, and both found a much higher proportion than expected of men: 47% in the former study and 45% in the latter. These figures are much closer to those of the present study which also deals with early rheumatoid disease. However, the near equal sex incidence in our study is not seen in the early presenters only.

The reason for the high proportion of men in the studies of early rheumatoid disease is not known. Otten and Boerma concluded that the disease occurred with equal incidence in the sexes but that men tended to improve while women went on to develop a more chronic form. However, the reason may lie in the sampling problems which are inherent in studies based on hospital populations, or there may be social reasons which make men present earlier with a disease which may threaten a job. Whatever the explanation, it is obvious that a different view is obtained when the disease is followed from its earliest stages.

The high frequency of first symptoms in the winter and autumn months has received only occasional comment. Loxton (1959) found that 93 of the 137 patients he questioned could state the month of onset. 69 of these developed arthritis in the period between October and March, with the highest

incidence in October and February. The mean number of onsets per month in this period was 11.5 compared with 4 in the remainder. He concluded that rheumatoid arthritis starts approximately three times more often in the colder months. Jacoby and others (1973) found that 43 patients out of 100 developed their first joint symptoms between December and February. December was worst with 22 onsets. While investigating the incidence of past polyarthritis in an epidemiological study of the population of Leigh, Lawrence (1965) found that the onset of such episodes occurred much more frequently in the winter months. The highest incidence appeared to be from December to March. Furthermore, Short and others (1957) reported a greater frequency of exacerbations in winter in established rheumatoid arthritis. The reason for the high incidence of onset in these months is not known, but gives rise to conjecture on the place of environmental and infective factors in the aetiology of rheumatoid disease.

The finding that the majority of rheumatoid patients have a slow, insidious onset of joint symptoms agrees with other reports. Jacoby and others (1973) subdivided the type of onset into 'acute' (if it could be dated by the patients to a specific day), 'subacute' (if the onset could be dated only to the nearest week), and 'gradual' (if it could be dated only to the nearest month). They found that 49 of their 100 patients had a 'gradual' onset, 23 patients had an 'acute' onset, and 28 'subacute'. Short and others (1957) divided the type of onset into acute and gradual with 21.8% of patients having an acute onset and 78.2% a gradual onset. However, Egelius, Havermark, and Jonsson (1949) found that the 'characteristic' type of rheumatoid arthritis, with slow insidious onset and progressive course, occurred in only 37.5%, concluding that it was not as typical as previously thought.

Others have attempted to describe the site of onset of joint symptoms. Sclater (1943) studied a group of 388 patients in whom he found an onset in the finger joints in 38% of female patients and in 26% of males. Egelius and others (1949) found an insidious, symmetrical onset in finger joints in 37.5% of the 200 patients they described. Jacoby and others (1973), in their series of 100 cases, described onset in the hands and wrists in 43%, ankles and feet in 21%, knees in 13%, and shoulders in 9%. Even though information in our study was taken very early in the course of the disease it was found that patients were not able accurately to describe onset in the individual small peripheral joints. However, the high incidence in hands and feet is common to all studies. It appears also that the upper limb is more commonly affected than the lower. Other workers do not seem to describe the initial multiple joint involvement that is seen in

the present study, where 29 patients have more than one joint involved and, furthermore, 15 patients have both upper and lower limbs involved.

It is of interest that a more rapidly severe disease, as measured in the first year by the presence of erosions, a large number of ARA criteria, or a poor functional grade, is indicated by a slow onset, initial involvement of the feet, and early progression to symmetry. The prognostic value of the features studied here has also been assessed regarding the long-term outcome measured clinically after a mean 4.5 years from onset. A worse prognosis was related to older age, and, to a lesser extent, to a slow onset and to symmetrical involvement within the first year.

That older patients do worse may be due to the problems caused by even a mild, early loss of function in an aging population. Sex did not influence outcome in our study, a finding at variance with others who suggest that males, at least in the early stages, do better (Cecil and Archer, 1926; Short and Bauer, 1948; Bywaters and Dresner, 1952;

Duthie and others, 1955; Otten and Boerma, 1959; Jonsson, 1961). Furthermore the literature indicates strongly that a prognosis is associated with early presentation (Buckley, 1936; Steinbrocker, 1946; Otten and Boerma, 1959; Ragan and Farrington, 1962; Sharp and others, 1964). We could not confirm this. 43 of our patients presented within 3 months and they fared no better than the remainder. Symmetry of joint involvement at onset had no prognostic value, but if symmetrical involvement occurred within the first year there was a strong trend for these patients to do worse, supporting the impression that the asymmetric form of the disease is less severe (Short and Bauer, 1948; Bywaters and Dresner, 1952). There is a similar trend for those with an insidious onset to fare worse than those with an abrupt onset which is in general agreement with other workers (Duthie and others, 1955; Jonsson, 1961; Sharp and others, 1964; Wawrzynska-Pagowska and others, 1970). The 3 with a palindromic onset also pursued a severe course.

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