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Early rheumatoid disease

II. Patterns of joint involvement

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Fleming, A., Benn, R. T., Corbett, M., and Wood, P. H. N. (1976). *Annals of the Rheumatic Diseases*, **35**, 361–364. **Early rheumatoid disease. II. Patterns of joint involvement.** Data from the first research clinic visit (Fleming and others, 1976) have been subjected to factor analysis to identify early patterns of joint involvement. Nine patterns emerged. Two patterns, if present early, were found to have prognostic significance. An eventually more severe disease was associated with a pattern of large joint involvement (shoulder, elbow, wrist, knee) and a pattern based on metatarso-phalangeal joints I and III.

Several studies have described the incidence of involvement of particular joints in early rheumatoid arthritis (RA) (Rotes-Querol and Roig-Escofet, 1968; Jacoby, Jayson, and Cosh, 1973; Fleming, Crown, and Corbett, 1976). A simple description of frequency, however, gives no indication of the various patterns of involvement which are seen. In RA there is considerable variation in the distribution of joints affected. While the human brain is sophisticated at perceiving patterns, this is difficult to quantify, and the problem of pattern identification in multilocus involvement has received in the past only anecdotal attention. It is possible that particular patterns and their association with other clinical features may go unnoticed. These difficulties are amenable to mathematical treatment.

This study of joint involvement in the earliest stages provides data which have been analysed to describe patterns of joint involvement, and their relationship to age, sex, presence of the rheumatoid factor, erosive status, and outcome. The tool used was factor analysis.

Patients and methods

These are as described in the preceding article (Fleming and others, 1976). The data were transferred to 80 column punch cards for subsequent computer processing, utilizing the facilities of the Manchester Regional Computer Centre. Analysis employed the Statistical Package for the Social Sciences (SPSS; Nie, Bent, and Hull, 1970). This suite contains a program for factor analysis to the requirements of this study.

Factor analysis is a statistical procedure used here to identify patterns of joint involvement. The postulate of factor analysis in this case is that the total joint involvement can be explained by a combination of different patterns. These patterns, or factors, are groups of joints which tend to be affected together.

In more statistical terms these factors represent groups of joints which are together more correlated than with other joints. The contribution each individual joint makes to a factor is quantified by a 'rotated factor loading'. Factor loadings are normally related to correlation coefficients, and like these can range from -1 to $+1$. For each factor, loadings are calculated for each joint and only those with large positive or negative loadings are said to contribute significantly to that factor. Thus for each factor the major contributing joints can be identified.

Each of the different factors will go some way towards explaining the overall pattern of joint involvement. In statistical terms each factor will explain a certain amount of the total variation in joint involvement. To explain all the variations an excessively large number of factors may be needed, but in practice a substantial amount of the variations can usually be explained with a small number of factors. In the present study an analysis was originally performed with 12 factors, but after examination of the results it was decided to reduce the number to 9 since the remaining 3 appeared to be relatively unimportant.

As it was hoped to predict outcome, the basic joint data for this study were taken from the first research clinic visit, a mean 7·9 months after the onset of joint symptoms.

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Results

The total incidence of involvement of the various joints on both sides is shown in Tables I and II. By far the most commonly involved joints are the metacarpophalangeal (MCP) joints, the proximal interphalangeal (PIP) joints, and the wrists. These are followed by the metatarsophalangeal (MTP) joints and the shoulders. The hips and the lower spine are least often affected. The interphalangeal joints of the toes were not included in the analysis.

Table I *Frequency of joint involvement*

Joint	*Right*	*Left*	*Bilateral*
TMJ	11	6	5
Shoulder	37	42	30
Elbow	20	15	14
Wrist	60	57	48
MCP	65	58	52
PIP	63	53	45
DIP	20	14	13
Hip	5	3	1
Knee	35	30	24
Ankle	25	23	18
Midtarsal	8	13	6
MTP	48	47	43
Cervical spine	26		
Dorsal spine	4		
Lumbar spine	3		

TMJ=Temporomandibular joint; MCP=metacarpophalangeal; PIP=proximal interphalangeal; DIP=distal interphalangeal; MTP=metatarsophalangeal.

Data were then submitted to factor analysis. The 9 factors derived by this procedure are shown in Table III, together with the loading of the individual joints. These factors describe group involvement of different joints, and they account for 63% of the total variation. In this analysis it was noted that the joints on the right and left sides behaved in like fashion.

For every patient factor estimates were then computed for each of the 9 factors in turn. These were estimates of how large a part each factor played in the pattern of joint involvement in the particular individual. This was done by computing the proportion of joints involved in the patient for the group of joints described by the factor. Thus a patient with four of the eight MTP joints involved would have a factor estimate of 0·5 for factor I.

These factor estimates were tested for possible associations and those showing significant associations are set out in Table IV. The pattern of joint involvement characterized by shoulder-elbow-wrist-knee was seen more often in the older age groups. This factor was also associated with seropositivity and with a more serious outcome. Involvement of MTP I and II was similarly associated with seropositivity and more severe disease, and also with erosions, but there was no relationship with age. On the other hand involvement of MTPs II–V was more striking in younger people and was associated with a better outcome. Involvement of MCPs II–V and of ankle-midtarsal joints showed some association with erosive changes.

Plotting joint involvement according to loadings on selected pairs of factors gives a diagrammatic representation of these pattern subgroups. This can

Table II *Frequency of particular small joint involvement*

	MCP		*PIP*		*DIP*		*MTP*	
	R	*L*	*R*	*L*	*R*	*L*	*R*	*L*
1st	28	24			16	11	21	20
2nd	53	46	43	38	8	7	31	33
3rd	51	46	51	41	10	4	36	36
4th	18	15	34	28	5	2	33	29
5th	12	9	17	23	20	14	25	25

Table III *9 factors and the loadings of individual variables*

Factor	*Loading of variables**			
(1) MTP II–V	II R0·73 L0·65	III R0·77 L0·83	IV R0·85 L0·89	V R0·77 L0·76
(2) DIP I–III	I R0·60 L0·80	II R0·87 L0·84	III R0·75 L0·74	
(3) PIP II–V	II R0·73 L0·80	III R0·69 L0·77	IV R0·60 L0·69	V R0·60 L0·40
(4) MCP II–V	II R0·58 L0·60	III R0·68 L0·59	IV R0·72 L0·67	V R0·70 L0·64
(5) SEWK†	S R0·44 L0·60	E R0·52 L0·56	W R0·64 L0·62	K R0·62 L0·58
(6) Ankle and midtarsal	Ankle R0·66 L0·62	Midtarsal R0·63 L0·77		
(7) Spine	Cervical 0·44	Dorsal 0·78	Lumbar 0·69	
(8) DIP IV–V	IV R0·53 L0·77	V R0·76 L0·85		
(9) MIP I–II	I R0·85 L0·82	II R0·51 L0·47		

* Only rotated loadings of at least 0.4 are shown.
† Shoulder (S), elbow (E), wrist (W), knee (K).

Table IV *Average factor estimates (mean frequency of joint involvement related to other variables. Only factors with significant associations are shown*

Factor (joint group)	Age in decades						Outcome		
	–24	–34	–44	–54	–64	–74	Improved	Mild	Severe
(1) MTP II–V	0·38*	0·38	0·36	0·37	0·28	0·14	0·16	0·43	0·35
(4) MCP II–V	0·33	0·23	0·13	0·30	0·42	0·35	0·21	0·35	0·34
(5) SEWK	0·29	0·27	0·29	0·34	0·43	0·49†	0·24	0·40†	0·42
(6) Ankle and midtarsal	0·25	0·13	0·25	0·11	0·19	0·15	0·14	0·18	0·18
(9) MTP I–II	0·08	0·29	0·34	0·35	0·20	0·15	0·09	0·32†	0·32†

Factor (joint group)	Rheumatoid factor		Joint erosions	
	Positive	Negative	Present	Absent
(1) MTP II–V	0·34	0·25	0·32	0·29
(4) MCP II–V	0·34	0·26	0·35*	0·23
(5) SEWK	0·41†	0·29	0·39	0·34
(6) Ankle and midtarsal	0·16	0·18	0·21*	0·09
(9) MTP I–II	0·32†	0·15	0·31†	0·15

Significance assessed by F. test for outcome and by t test for other variables.
Probability values, P * < 0·10, † < 0·05.

be seen in the Figure where the horizontal axis represents loadings on the first factor (MTPs II–V) and the vertical axis those on the second factor (PIPs I–III). Thus it can be seen that joint involvement in this instance divides itself into three major groups: MTP joints, which are involved in one syndrome process; DIP joints, which are involved in another syndrome process; and the remainder of the joints, which are not appreciably involved in either of these syndrome processes. This spatial representation of subgroups can be shown for each pair of factors.

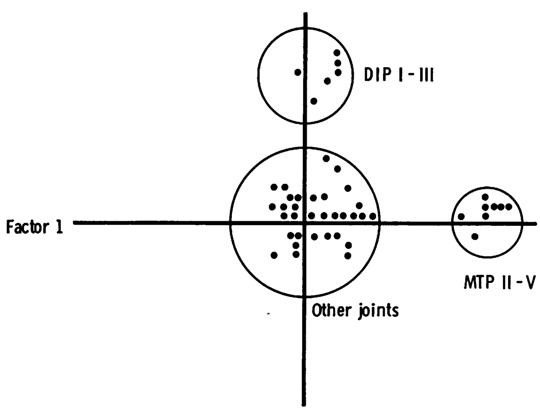

FIGURE *Spatial representation of factors 1 and 2*

Discussion

It is of interest that this study identifies subgroups of joint involvement which are not unexpected, and which seem to lend numerical justification for previously recognized patterns which for the most part have received only anecdotal description. While most patterns emerge fairly clearly with regard to the loadings on the involved joints, there were some overlap phenomena. This was seen in the pattern of involvement of PIPs II–V where much lower but nonetheless clear loadings were found on MCPs I–III.

That rheumatoid arthritis is predominantly a disease of peripheral joints is confirmed, not only by the high frequency of involvement of the small joints of the hands and feet, but also by the large number of identifiable patterns (6 out of 9) formed by the clusterings of these small joints. Furthermore, differential involvement of some joints in certain groups was observed. Thus there was one subgroup of involvement of MTPs I–II, and another involving MTPs II–V. Similarly there was one subgroup showing involvement of finger DIPs I–III and another of DIPs IV–V.

Two particular patterns seem to have a predilection for different age groups. The pattern of involvement based on lateral MTP joints (MTPs II–V) occurred in a younger age group, while that based on larger proximal joints the shoulder-elbow-wrist-knee was seen more often in the older patient.

A more severe disease state as measured by the presence of erosions and a positive sheep cell agglutination test was seen in the pattern which included MTPs I–II, and, to a lesser extent, the large proximal joint pattern and that involving the lateral MCPs.

Little previous work has suggested that a particular site or pattern of joint involvement in the early stages of rheumatoid arthritis is of prognostic significance (Otten and Boerma, 1959; Ragan and Farrington, 1962), although Wawrzynska-Pagowska and others (1970) found that involvement at the onset of the disease of hand and/or feet only was of ominous significance in the development of erosive disease. However, it is clear from the present study, where pattern of involvement was correlated with outcome assessed clinically 4·5 years from onset, that early patterns based on involvement of large proximal joints and of MTPs I–II indicate the likelihood of a poorer prognosis and may help the physician in predicting outcome.

Thus, factor analysis of data on the site of joint involvement in a group of patients seen approximately 8 months after onset of RA provides numerical justification for the patterns of joint involvement most commonly seen in the early stages of the disease, and helps assessment of the significance of these patterns.

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