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The arthritis of Behçet's disease: a prospective study

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SUMMARY A prospective study of arthritis was performed in 47 patients with Behçet's disease followed up over a 47-month period (mean 19·15 months, SD 14·09). These patients had a total of 80 episodes of arthritis, which were analysed for joint distribution and symmetry, in 56 of which the duration could also be determined. Attacks were oligoarticular, affecting up to 4 joints per patient, 54 (68%) being monoarticular. Knees, ankles, and wrists were the most commonly involved joints. Involvement of spinal, shoulder, hip, and sacroiliac joints was rare. The arthritis was usually not deforming and subacute; 82% (46/56) of the attacks lasted for 2 months or less and 18% (10/56) for between 3 months and 4 years. The ESR was moderately elevated during the attacks. In 32 specimens the synovial fluid was inflammatory (cell count $14·7 \pm 10·1 \times 10^9$/l), but in 19 (59%) a good mucin clot formed. Synovial biopsy in 12 patients revealed superficial ulceration, paucity of plasma cells, and in 5 instances lymphoid follicle formation.

Hulusi Behçet defined Behçet's Disease (BD) in 1937 as a triple symptom complex of aphthous stomatitis, genital ulceration, and iritis.[1] A year later he reported that 'rheumatoid pains' might also occur.[2] Since then there have been many articles reporting joint involvement in BD,[3–8] which were recently reviewed by Barnes.[8]

We have had the unique opportunity of examining prospectively the arthropathy of this disease in more detail in a multidisciplinary BD outpatient clinic.

Material and methods

A multidisciplinary weekly BD outpatient clinic was instituted in 1977 at the Cerrahpaşa Medical Faculty of the University of Istanbul attended by 2 rheumatologists, 2 haematologists, 2 dermatologists, and 2 ophthalmologists. One rheumatologist (S.Y.) is responsible for the primary care of the patients.

Patients are referred on the clinical suspicion of BD either from within the 2000-bed teaching hospital or from outside physicians. Diagnostic criteria as proposed by O'Duffy[9] are used, requiring 3 of the following 5 features present either previously or at first attendance: aphthous stomatitis, genital ulceration, dermal vasculitis, uveitis, or arthritis. Either aphthous stomatitis or genital ulceration has to be present. The clinical observation of pyoderma and/or erythema-nodosum-like lesions is considered adequate for the diagnosis of dermal vasculitis.

All patients have a routine slit-lamp examination of the eyes at each visit.

One hundred and eighty-four patients have attended the clinic, of whom 71 (39%) have had arthritis as part of their disease. In this study we analyse the data on 47 of the 71 who developed or had an exacerbation of arthritis during a 47-month follow up period, that is, the prospective arthritis group. These 47 patients attended the clinic on a total of 467 occasions (mean 9·94, SD 8·66 visits per patient) over a mean period of 19·15 months (range 1–47, SD 14·09).

Excluded from the formal analysis are the 29 patients (16%) with arthralgia alone, since this cannot be quantified.

As previously reported,[10] a full blood count and erythrocyte sedimentation rate (ESR) (Westergren) were performed at each visit. Exacerbations

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and remissions of arthritis were observed in 31 patients, the mean ESR in periods of exacerbation and remission in each patient being compared by the *t* test for paired data. The former mean was also compared with the mean ESR of patients without arthritis by the *t* test for independent groups.

C-reactive protein (CRP) and latex rheumatoid factor determinations were performed by slide agglutination techniques (Behringwerke, Germany). Thirty-two of the 47 patients with arthritis had CRP determinations (72 determinations). In 9 of these patients the determinations were done both during active arthritis and quiescent periods (39 determinations). In addition CRP results during an arthritic attack (32 attacks among 24 patients) were compared with those in patients without joint involvement (26 determinations among 12 patients). The results were compared by χ^2 analysis.

Latex tests were performed on 32 patients with arthritis (63 determinations). Antinuclear antibody estimation was performed on 23 patients with arthritis by indirect immunofluorescence with human leucocytes as nuclear substrate and fluorescein anti-IgP (Behringwerke, Germany).

Thirty-two specimens of synovial fluid from 17 patients were available for analysis. Synovial biopsy of the knee was performed on 12 patients, by open biopsy in one case and with a Parker-Pearson needle[11] in the remainder. The sections were stained with haematoxylin and eosin (H–E),[12] and in 8 specimens with pyronin[13] for the detection of plasma cells.

Radiographs of joints were taken as clinically indicated. Anteroposterior radiographs of the pelvis were taken in 44 patients irrespective of back symptoms to survey the prevalence of sacroiliitis. The findings in this study have been published elsewhere.[14]

Histocompatibility typing was performed on 145 patients by the standard techniques.[15 16]

A positive pathergy test, nonspecific hypersensitivity to needle prick, was defined as the development of a papule 48 hours after a sterile needle prick which penetrated the corium at an avascular site in the forearm. Erythema alone at the site of the needle prick was considered a negative result.[17]

Statistical methods included the χ^2 test, analysis of variance, and Student's *t* test for independent groups and dependent groups.

Results

The mean age and sex distribution of the patients, and the frequency of the major clinical findings including thromboplebitis, are shown in Table 1. Clinical features in those patients with joint involvement did not differ significantly when compared with those without joint involvement, except that erythema nodosum occurred more frequently and the incidence of the HLA B5 antigen was higher in patients with arthritis.

Among the 47 patients with arthritis studied prospectively, in only 6 (patients 8, 27, 28, 29, 32, 47) was

Table 1 *Age, sex, and major clinical findings of the patients with and without joint involvement*

	Prospective arthritis group		*Retrospective group*		*No joint involvement*	
			Arthritis n=24	*Arthralgia n=29*		
No. of patients	*47*		*53*		*84*	
Sex (male:female)	9:38		17:36		23:61	
Age (years ±SD)	32·89±8·52		31·90±8·23		33·08±8·69	
(range)	20–56		16–51		16–67	
Aphthous stomatitis	47	(100)	53	(100)	84	(100)
Genital ulcer	41	(87)	48	(91)	72	(86)
Folliculitis	43	(91)	46	(87)	67	(80)
E. nodosum*	33	(70)	31	(58)	42	(50)
Uveitis	20	(43)	34	(64)	46	(55)
Thrombophlebitis	15	(32)	12	(23)	23	(27)
Pathergy: positive	44	(98)	46	(92)	77	(94)
negative	1	(2)	4	(8)	5	(6)
HLA B5† positive	34	(83)	31	(84)	43	(64)
negative	7	(17)	6	(16)	24	(36)

Percentages in parentheses.
*Erythema nodosum: Arthritis versus no joint involvement: $\chi^2=4·23$, $p<0·05$; joint involvement versus no joint involvement: $\chi^2=3·11$, $0·10>p>0·05$.
†HLA B5: Arthritis versus no joint involvement: $\chi^2=3·50$, $0·10>p>0·05$; joint involvement versus no joint involvement: $\chi^2=5·99$, $p<0·02$.

arthritis one of the 3 symptoms necessary for those patients to fulfil O'Duffy's diagnostic criteria.

Table 2 shows the clinical and laboratory features and the various aspects of joint involvement in the 47 patients in the 'prospective arthritis' group. Involved joints were warm and swollen, but redness of the overlying skin was not observed. Mild morning stiffness, lasting up to a maximum of half an hour, was reported by 16 (34%) patients. The arthritis was not associated with deformity except in one patient who had mild limitation of dorsiflexion of the wrists (patient 29).

During the follow-up of these 47 patients there were 80 arthritic episodes affecting one or more joints per patient. The distribution and symmetry of the joints involved were analysed during these attacks. The arthritis was monoarticular (Fig. 1) in 54 of the 80 attacks. In the remainder the mean number of joints involved per patient was 3. The maximum number of joints involved during an attack was 5, occurring in only 2 patients. The number of joints involved in the 80 episodes of arthritis is shown in Table 3. The frequency in which the different joints were involved is shown in Fig. 2. The knee was the commonest joint involved followed by the ankle, wrist, and elbow. Shoulder and hip involvement was uncommon.

Only one patient had spinal arthritis and definite sacroiliitis.[14] This 29-year-old man had all 5 manifestations of BD as required by O'Duffy's criteria and

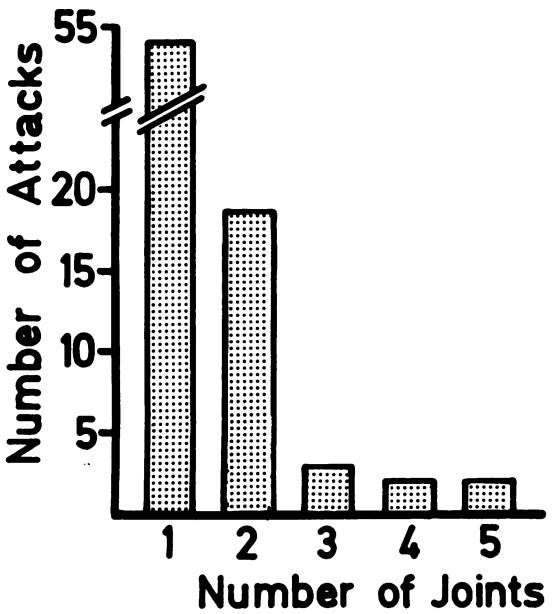

Fig. 1 *Number of joints involved during an attack.*

Table 3 *Distribution of joints involved in 80 attacks of arthritis in the 47 patients studied prospectively*

Number of attacks	*Number of joints involved and symmetry*
Monoarticular 54	
Oligo- and polyarticular 26	16: 2 symmetrically
	3: 2 asymmetrically
	3: 3 (1 pair symmetrically + 1 other joint)
	2: 4 (2 pairs symmetrically, 1 pair symmetrically +2 asymmetrically)
	2: 5 (2 pairs symmetrically + 1 other joint)

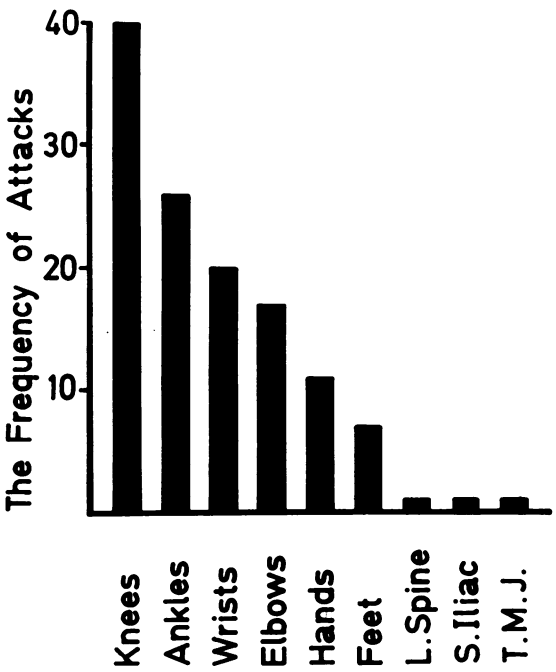

Fig. 2 *Distribution of the joints involved.*

was HLA B27 positive, B5 negative, and had a positive pathergy test (patient 37). We believe he had concomitant ankylosing spondylitis and Behçet's disease. Two patients had Achilles tendinitis, one of whom had bilateral calcaneal erosions. One patient had subcutaneous nodules, which has been reported previously.[18]

The duration of 56 attacks of arthritis in 37 patients could be analysed and is shown in Fig. 3. Forty-six (82%) attacks lasted for 2 months or less, the shortest episode being 3 days in one patient

Table 2 *Individual clinical findings, disease duration, pathergy, and HLA B5 status of the 47 patients with arthritis followed prospectively*

Patient no.	Sex	Age	Clinical findings								HLA B5	Number of visits	Follow-up (months)	Hand		Wrist	
			Aphthous stomatitis	Genital ulceration	Folliculitis	Erythema nodosum	Arthritis	Uveitis	Thrombophlebitis	Pathergy				R	L	R	L
1	M	28	+	+	+	−	+	+	−	+	+	21	34	−	−	1	**1**
2	M	35	+	+	−	+	+	−	+	+	+	4	6	−	1	−	−
3	M	36	+	+	+	+	+	+	+	+	+	24	39	−	−	−	−
4	M	23	+	+	+	−	+	+	−	−	+	1	1	1	−	−	−
5	M	30	+	+	+	+	+	+	−	+	+	19	36	1	1	−	−
6	M	27	+	+	+	+	+	−	−	+	+	6	32	−	−	−	−
7	M	29	+	+	+	+	+	−	+	+	+	6	27	−	1	−	−
8	M	28	+	+	−	−	+	−	−	Ø	Ø	1	1	−	−	−	−
9	M	33	+	+	+	+	+	−	−	+	Ø	3	3	1	−	−	−
10	M	36	+	+	+	+	+	−	+	Ø	+	11	12	−	−	**3**	**2**
11	M	45	+	+	+	+	+	+	+	+	+	12	27	−	−	−	−
12	M	48	+	+	+	+	+	−	+	+	−	13	29	1	−	−	−
13	M	35	+	+	+	+	+	−	−	+	+	6	13	−	−	−	−
14	M	24	+	+	+	−	+	−	−	+	Ø	4	4	−	−	−	−
15	M	25	+	+	+	−	+	+	−	+	+	12	37	−	−	−	−
16	M	25	+	+	+	+	+	+	+	+	+	16	41	−	−	−	−
17	M	42	+	+	+	+	+	−	−	+	+	10	27	−	−	−	−
18	M	29	+	+	+	+	+	−	−	+	+	6	11	−	−	1	−
19	M	40	+	+	+	+	+	+	−	+	+	33	47	−	−	−	−
20	M	56	+	+	−	+	+	−	+	+	+	2	2	−	−	−	1
21	M	20	+	+	+	+	+	+	+	+	+	6	6	−	−	−	−
22	M	32	+	+	+	+	+	−	+	+	+	2	2	**1**	−	−	−
23	M	46	+	+	+	+	+	+	+	+	+	9	19	−	−	1	−
24	M	31	+	+	+	+	+	−	−	+	+	11	24	−	−	−	−
25	M	23	+	+	+	+	+	+	−	+	+	6	28	−	−	−	−
26	M	29	+	+	+	+	+	−	+	+	+	7	19	−	−	−	−
27	M	30	+	−	+	−	+	−	−	+	Ø	2	2	−	−	−	−
28	M	38	+	−	+	+	+	−	−	+	+	10	22	−	−	−	−
29	M	38	+	−	+	+	+	−	−	+	−	8	22	−	−	**1**	**1**
30	M	44	+	+	+	+	+	−	−	+	−	21	37	−	−	−	−
31	M	20	+	+	+	+	+	+	−	+	+	33	45	−	−	−	−
32	M	34	+	−	+	−	+	−	−	+	+	3	10	−	−	−	−
33	M	31	+	−	+	−	+	+	−	+	+	10	18	−	−	−	**1**
34	M	29	+	+	+	−	+	−	+	+	Ø	7	13	−	−	−	−
35	M	34	+	+	+	+	+	+	+	+	+	21	32	−	−	−	−
36	M	23	+	+	+	−	+	−	−	+	−	5	9	1	−	1	−
37	M	29	+	+	+	−	+	+	−	+	−	6	10	−	−	−	−
38	M	23	+	+	+	+	+	+	+	+	+	4	29	−	−	−	−
39	F	30	+	+	+	+	+	+	−	+	+	28	35	−	−	2	−
40	F	31	+	+	+	+	+	+	−	+	+	12	27	−	−	−	−
41	F	32	+	+	+	+	+	+	−	+	−	28	36	**X**	**X**	**X**	**X**
42	F	38	+	+	+	−	+	−	−	+	−	1	1	−	−	−	−
43	F	22	+	+	+	+	+	−	−	+	+	3	5	−	−	−	−
44	F	50	+	+	+	+	+	−	−	+	+	3	6	−	−	−	1
45	F	51	+	+	+	−	+	−	−	+	Ø	2	1	−	−	1	−
46	F	36	+	+	+	−	+	+	−	+	+	8	12	−	−	−	−
47	F	28	+	−	−	+	+	−	−	+	+	1	1	−	−	−	−

Ø: not done.
TMJ: temporomandibular joint. SI: sacroiliac joints.
R: right. L: left.
Bold type indicates the joints involved during the most polyarthritic attack.
Numbers indicate arthritic attacks.
X: this patient uniquely had numerous very frequently repeating episodes of symmetrical peripheral small and large joint arthritis involving mostly 5 joints or less at a time lasting up to one week. Thus her attack in any one joint was evaluated as chronic affliction of that joint.
Hand: involvement of proximal interphalangeal joints (4 patients) and metacarpophalangeal joints (5 patients); terminal interphalangeal joints not involved.

Elbow		*Shoulder*		*Neck*	*TMJ*		*Back + SI*	*Hip*		*Knee*		*Ankle*		*Foot*	
R	*L*	*R*	*L*		*R*	*L*		*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*
3	**3**	–	–	–	–	–	–	–	–	–	–	**1**	1	–	–
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–	–	–	–	–	–	–	–	–	–	1	–	–	–	–	–
–	–	–	–	–	–	–	–	–	–	**2**	**1**	–	–	–	–
–	–	–	–	–	–	–	–	–	–	**4**	**1**	–	–	1	–
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1	**1**	–	–	–	–	–	–	–	–	**1**	**1**	–	–	–	–
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1	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
–	–	–	–	–	–	–	–	–	–	–	2	–	–	–	–
–	–	–	–	–	–	–	–	–	–	–	2	–	–	–	–
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–	–	–	–	–	–	–	–	–	–	–	–	1	**2**	**1**	**1**
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1	**1**	–	–	–	–	–	–	–	–	2	–	–	–	–	–
–	–	–	–	–	–	–	–	–	–	–	–	–	1	–	1
–	–	–	–	–	–	–	–	–	–	–	–	**1**	**3**	–	–
X	**X**	–	–	–	–	–	–	–	–	**X**	**X**	**X**	**X**	–	–
1	**1**	–	–	–	–	–	–	–	–	**1**	**1**	–	–	–	–
–	–	–	–	–	–	–	–	–	–	–	–	–	–	**2**	**1**
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–	–	–	–	–	–	–	–	–	–	**2**	**1**	–	–	–	–
–	–	–	–	–	–	–	–	–	–	–	–	–	1	–	–

(number 2), although chronic cases lasting several months—up to 4 years—occurred. The duration of the remaining 24 attacks (in 10 patients) could not be assessed because of difficulty in follow-up.

Table 4 shows the results of laboratory investigation. The ESR was significantly, but only moderately raised during exacerbations in comparison with quiescent periods in patients with arthritis, but patients with arthritis had a significantly higher ESR than patients without joint involvement. The CRP was positive significantly more often during an arthritic attack than in patients with no joint involvement. In 32 patients with arthritis latex rheumatoid factor tests were negative on 60 occasions, and positive on 3 occasions in 3 patients. ANA was also negative in 23 patients. Of the 145 patients on whom tissue typing was performed 108 carried the B5 and 9 the B27 antigens.

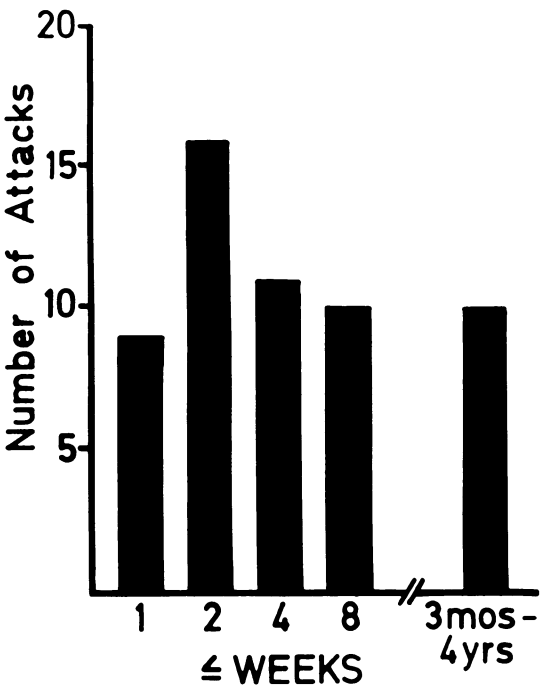

Fig. 3 *Duration of the arthritic attacks.*

Table 5 shows the results of synovial fluid investigations. Synovial fluid was of inflammatory type with a predominance of polymorphonuclear leucocytes. However, a good mucin clot was formed in the majority (19/32, 59%) of specimens.

Synovial biopsy findings are summarised in Table 6. Involvement of the superficial layer was present without plasma cell infiltration, even in the 5 specimens where there was distinct germinal follicle formation. Initially we were unable to observe any plasma cells in H–E stained sections, but some were visible in 8 specimens stained with pyronin. Taking the counts in all high-powered fields together, we found a mean of 4·7, SD 5·3, range 0–15, plasma cells in 7 specimens. One specimen had an average of 4 plasma cells per high-powered field.

In 5 patients radiographic erosive changes were noted. They included erosion of both calcanea without sacroiliitis, of both first and second metatarsophalangeal joints (Figs. 4, 5), of one temporomandibular joint with recurrent arthritis at the same joint, of the metatarsophalangeal and proximal interphalangeal joints of the feet, and cystic changes in the shaft of the middle phalanx of one hand, each in one patient.

Table 7 summarises the drug therapy used in 44 (55%) of the 80 observed attacks of arthritis. For the remaining 36 episodes no medication was given. Intra-articular steroids seemed to be beneficial on the first 2 occasions,[19] but subsequent experience proved them to be ineffective.

Table 4 *Laboratory results*

		All arthritis		*Arthritis*			*No joint involvement*	
		n		*n*	*Remission*	*Active*	*n*	
ESR	(mm/h)			31	18·72±14·87*	30·79±21·91****	79	20·27±17·74**
CRP	positive		35		7†	8†		
	negative	32	37	9	18†	6†		
	positive			24		20††	12	6††
	negative					12††		20††
Latex	negative	29	60					
	positive	3	3					
ANA	negative	23	23					

n=number of patients tested, some being retested on multiple occasions.
* $t=2·02$: $0·10>p>0·05$.
** $t=2·61$: $p<0·01$.
† $\chi^2=2·1$: $p>0·05$.
†† $\chi^2=7·41$: $p<0·01$.

Table 5 *Synovial fluid findings (17 patients; 32 specimens)*

Case no.	*Knee*	*Appearance**	*Viscosity*	*Mucin clot*	*Leucocytes*	*PMN†%*	*Glucose mg/dl*	
							Blood	*Synovial*
16	Left	Cloudy	+	+++	25600	93	60	50
14	Right	Cloudy	+	+++	5600	64	158	141
15	Right	Cloudy	+	++	22600	97	76	10
	Right	Cloudy	+	++	33700	94		
	Right	Cloudy	++	+++	25200	97		
	Right	Cloudy	+++	++++	36200	92		
18	Left	S. Cloudy	++++	++++	300	3		
	Left	Cloudy	+	+++	17400	98		
19	Left				1600	25		
	Left	S. Cloudy	++	++	2200	22	65	87
	Left	Cloudy	++	+++	15200	99		
41	Right	Cloudy	+	+	13000	45	65	72
	Right	Cloudy	+	++	25400	95	90	75
	Left	Cloudy	++	++	14400	88	90	75
	Right	Cloudy	+	+	29600	97		
	Left	Cloudy	+	++	16600	97		
22	Left	Cloudy	+	+	12800	69	62	60
42	Left	Clear	++++	++++	5800	88		
25	Left	Cloudy	++++	++++	8000	75		
	Left	Cloudy	++++	++++	5100			
27	Right	Cloudy	+	+	29000	89		
33	Right	Cloudy	++	+++	14300	95		
17	Right	S. Cloudy	++	++	2400	46		
	Right	Cloudy	+++	++++	12400	95		
36	Right	Cloudy	+++	+++	8700	100		
26	Left	Cloudy	++++	++++	5900	85		
	Left	Cloudy	+++	+++	7000	77	74	63
46	Right	Cloudy	+	+++	29000	95		
	Right	Cloudy	++	+++	13500	58		
34	Right	Cloudy	++	+++	12700	92		
	Right	Cloudy	+	++	12600	90		
38	Right	Cloudy	++	++++	5500	90		

*S. Cloudy=slightly cloudy. †PMN: Polymorphonuclear leucocytes.
SI conversion: Number of leucocytes/mm^3 $\times 10^6$=number/l. Glucose mg/dl $\times$ 0·0555=mmol/l.

Discussion

This prospective study has enabled us to describe the arthritis of BD more precisely. The only previous study which assessed the number of joints involved in BD is that of Mason and Barnes,[5] who found a mean of 5·5 joints affected per patient. Zizic and Stevens state that arthritis is usually polyarticular without quoting the number of joints involved.[20] Our prospective series indicates that monoarticular arthritis is more common in BD. The figure of 5·5 joints per patient in the Mason and Barnes series might reflect inclusion simply by a history of arthritic attacks, the inclusion of arthralgia, or a different pattern of arthritis in Britain. It is recognised that this disease has differing manifestations in different parts of the world.[21 22] Further if one takes the traditional concept of 5 or more joints per patient as being polyarticular, the figure of 5·5 joints per patient is only marginally polyarticular.

We have found 2 opposing points of view on the symmetry of the arthritis in this disease. One is that of Barnes,[8] who states that joint involvement is symmetrical, the other is Chamberlain's,[6] who mentions asymmetrical involvement. Our larger experience indicates that joint involvement is usually symmetrical (when not monoarticular) and, as Barnes[8] has also pointed out, may resemble the joint involvement in rheumatoid arthritis. In our series 7 arthritic attacks in 5 patients involved both elbows and 4 attacks in 4 patients, both wrists, which is a very common presentation of rheumatoid arthritis.

The duration of arthritis in individual patients has previously been described by Mason and Barnes.[5] They recorded a subacute or chronic course without the episodic nature of the arthritis which we have observed, the majority of attacks in our series lasting 2 months or less. Although Mason and Barnes[5] mention that 80% of their patients had significant morning stiffness, this was found in only 34% (16/47) of

Table 6 *Synovial biopsy results*

Case no.	*Duration of arthritis* (yr)*	*Synovial cell hyperplasia*		*Villi*	*Synovial inflamation †*		*Superficial ulceration*	*Granulation tissue*
		Focal	*Diffuse*		*Superficial*	*Deep*		
16	0·3	+++	–	–	+	–	–	–
25	0·4	+++	–	–	+	–	–	–
18	4·0	++	+	+	+	–	–	–
15	2·5	–	–	–	–	Ø	++	++
19	3·0	–	–	–	+	–	++	++
17	0·7	++	–	–	+	Ø	+++	+++
41	3·0	+	–	–	+	–	+	–
33	0·3	++	–	–	Ø	Ø	++	–
34	0·5	+++	++	++	+	–	+	+
26	1·0	++	+	+	+	–	+	++
46	6·0	+++	–	–	+	–	++	++
36	0·4	+	–	–	+	–	+	–

*The stated time refers to the time elapsed from the onset of the first attack in the knee joint, which might have had more than one attack. In no instance had the biopsied joint been continuously inflammed for more than a month before the biopsy was done.
†Ø: Specimen not adequate for evaluation.

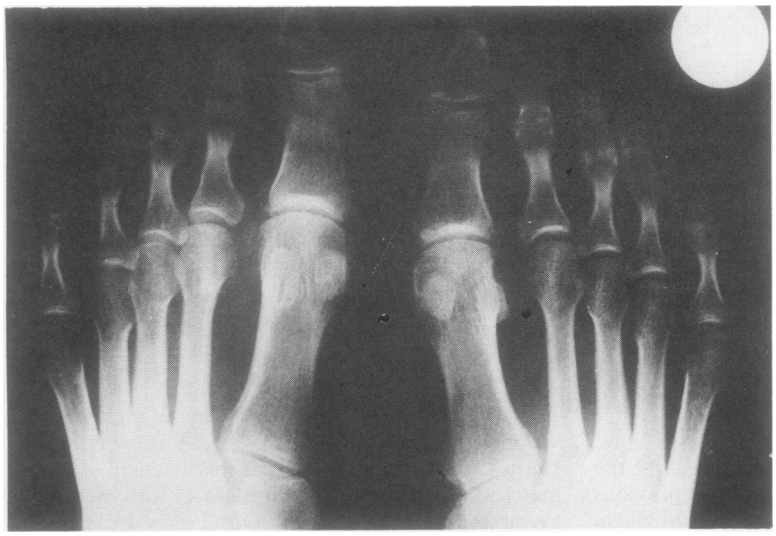

Fig. 4 *Erosion particularly in left metatarsophalangeal joint September 1979.*

our patients, and it was never as pronounced as in rheumatoid arthritis.

The arthritis of BD usually involved peripheral large joints. However, as has been previously observed, [4-6 8 23 24] patients commonly have involvement of wrists and elbows, but involvement of distal interphalangeal, spinal, or sacroiliac joints is very uncommon. The controversy over the possibility of sacroiliac involvement[5 6 25-27] has, we believe, now been resolved.[14] These features separate the arthropathy of BD from the group of seronegative spondarthritides.

Mason and Barnes found an elevated ESR in 13 of 19 patients with arthritis with a range of 24–114 mm per hour.[5] Shimizu *et al.* also mentioned an elevated ESR in 60 of 100 patients not all of whom had arthritis.[27] Neither group evaluated the ESR with respect to the clinical activity of the arthritis or the disease in general. The patients in our series with arthritis had an ESR on average 10 mm higher during exacerbations in relation both to periods of remission and to those patients without joint involvement. There were nevertheless patients with a normal ESR during periods of active arthritis.

Fibrin exudation		*Increased vascularity*	*Neutrophils*	*Lymphocytes*	*Plasma cells‡*		*Lymphoid follicles*
Superficial	*Deep*				*HE*	*P*	
–	–	++++	+	++	–	2	–
–	–	–	+	+	–	2	+
–	–	+	+	+	–	8	–
++	+	+	++	++	–	0	+
+	–	+	+++	+	–	ND	–
++	+	+	++	++	–	ND	–
+	+	–	+	++	–	15	+
+	–	–	++	+	–	ND	–
+	–	+	+++	++	–	ND	+
–	+	+	+++	+	–	1	–
++	–	+	++	++	–	20§	+
+	–	–	+	++	–	5	–

‡HE: Haematoxylin and eosin; P: Pyronin dye (see text); ND: Not done.
§A total of 5 high-powered fields were read.

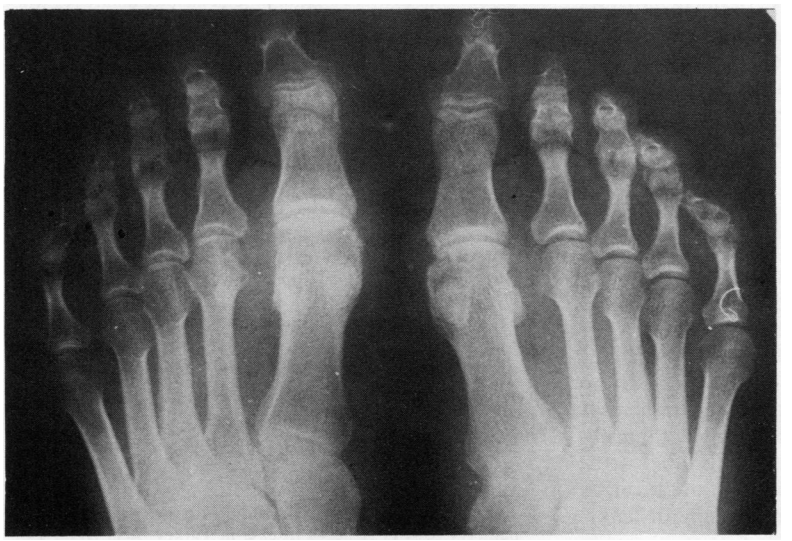

Fig. 5 *Same patient as in Fig. 4. Further erosion, February 1980.*

Table 7 *Drug therapies employed for arthritis*

Colchicine 1·5 mg/day	11 attacks
Azapropazone 900 mg/day	10 attacks
Salicylates 3 g/day	1 attack
Ibuprofen 1200 mg/day	2 attacks
Indomethacin 150 mg/day	4 attacks
Phenylbutazone 300 mg/day	3 attacks
Oral steroid 30–60 mg/day	3 attacks
Intra-articular steroids	10 attacks

Although a positive CRP was significantly more common during an arthritic attack than in patients with no joint involvement, it was not commoner in individual patients when exacerbations of arthritis were compared with remissions. Thus both ESR and CRP have a limited usefulness in following the arthritis of BD. The latex rheumatoid factor test (except for temporary positive results in 3 patients on 3 occasions) and ANA were negative in all patients tested, which is in agreement with other reports.[5 6 8 23 27] The sensitivity of the pathergy test continued to be high, as has been reported previously.[17 22]

One hundred and eight out of 145 patients carried the HLA B5 antigen, as we have previously reported.[22 28] The fact that HLA B5 was more frequent among the patients with joint involvement is further evidence that joint involvement is an integral part of this entity. Lehner reported a moderately increased prevalence of HLA B27 among patients with joint involvement.[29] We have not observed this. Nine of 145 (6%) of our patients carried HLA B27, a figure not significantly different from the 3% prevalence in our normal population.[30]

Synovial fluid analyses have been reported in 17 patients in 6 papers.[20 23 24 31-33] In 5 of these 17 (29%) cases the synovial fluid was reported as noninflammatory. Our series indicates that synovial fluid is almost always inflammatory, although usually a good mucin clot is formed. The usual inverse relationship between the synovial fluid cell count and the mucin clot test is not characteristically present in the arthritides of rheumatic fever and familial Mediterranean fever.[34 35] BD is yet another example in which a high synovial fluid cell count may be accompanied by a good mucin clot.

There have been relatively few reports on synovial histology in BD.[7 20 27 33] In 6 out of 12 (50%) specimens we have observed loss of the superficial cell layer, which was replaced by inflammatory granulation tissue. Gibson *et al.* recently reported,[33] however, that they had observed the replacement of the superficial cell lining by granulation tissue in only one of 7 specimens. In our series there was no involvement of the deeper layers of the synovium, and in only one specimen (patient 46) was there some increase in plasma cells detected by staining with pyronin. There was a striking paucity of plasma cells in the other specimens. Five biopsies showed lymphoid follicle formation. Our results of synovial histology are similar to those reported by Vernon-Roberts *et al.*[7]

Gibson *et al.*[33] also point out that the synovial changes in BD may be similar to those observed in early rheumatoid arthritis and, referring to the work of Schumacher and Kitridou,[36] to any synovitis of recent onset. We believe that this interpretation needs confirmation by studying greater numbers of specimens from patients with BD and comparing them with specimens from patients with other arthritides known to cause synovitis of short duration, as in familial Mediterranean fever and rheumatic fever.

Our uncontrolled experience in the treatment of the arthritides of BD has been disappointing. We believe that the traditional anti-inflammatory drugs are not of benefit. Our double-blind controlled experience with colchicine, as reported elsewhere,[37] indicates that this drug may improve arthralgia but not arthritis in this condition. Thus it is currently our practice to manage this arthritis, which is usually self-limiting, by waiting and reassurance.

In summary we believe that the arthritis of BD is unique among the arthritides. It is usually a non-deforming monoarticular or symmetrical oligoarthritis which is commonly subacute and self-limiting. The pattern of joint involvement is distinctly different from that of the seronegative spondarthritides. The synovial fluid is inflammatory, usually forming a good mucin clot. Synovial histology needs further study.

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Book review

Mercer's Orthopaedic Surgery. 8th Edn. By Robert B. Duthie and George Bentley. Pp. 1170. £75.00. Edward Arnold: London. 1983.

This is the eighth edition of an established orthopaedic textbook, which maintains its comprehensive account of locomotor disorders and their surgical management. Advances in bioengineering and radiology are included, although the impact of CT scanning could perhaps have been more fully evaluated. The text is well set out, with excellent line drawings and tables, although relatively few clinical photographs. The radiographs are, with a few exceptions, clearly reproduced. The initial sections are on a systematic pathological basis, and the later chapters cover the range of clinical disorders anatomically.

The book avoids the major defect of excessive overlap and repetition found in many large multiauthor texts. There is a clear index and an extensive bibliography at the end of each chapter. The price by present-day standards is reasonable. But should this be considered as an essential reference book for any rheumatology library? From the rheumatologist's viewpoint it would have been useful to have seen a greater emphasis on the importance of a team approach to the problems of the rheumatoid patient. There is insufficient appraisal of the planning of orthopaedic intervention as one episode in a continuing long-term management programme. The value of synovectomy is overemphasised. Simple errors appear in the section on 'Arthritis and rheumatic diseases'. Alclofenac is still mentioned as a first-line drug, penicillamine as an immunosuppressive agent, and phenylbutazone as a second-line drug. Furthermore it is worrying to see phenylbutazone advocated so prominently as a nonsteroidal agent, when considering the influence this may have on orthopaedic junior staff in particular.

These are, however, minor criticisms in a comprehensive and authoritative text, and as an up-to-date orthopaedic reference book it probably ranks as one of the best available.

J. D. PERRY