Joint hypermobility leading to osteoarthrosis and chondrocalcinosis

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SUMMARY We have reviewed 21 adults referred to a rheumatology clinic and considered to have generalised joint hypermobility by the criteria of Carter and Wilkinson (1964), modified by Beighton et al. (1973). They fell into two categories. 5 patients had a raised plasma viscosity (PV) and in each case a definite pathology was found to account for this, superimposed on hypermobile joints. The remaining 16 had a normal PV and this group was thought to represent the late natural history of hypermobility. 5 of these (aged 32 to 54 years) had no evidence of osteoarthrosis but the remaining 11 (aged 34 to 80 years) had widespread radiological osteoarthrosis. Synovial histology was obtained at arthroscopy in 6 of these patients and 4 (aged 60 to 75) had chondrocalcinosis. This previously undescribed finding may be the end result of hypermobile joints. Hypermobile patients with joint deformity (lax connective tissue), widespread synovial thickening (traumatic), and hot joint effusions (chondrocalcinosis) may mimic rheumatoid arthritis. They must be distinguished from patients who develop rheumatoid arthritis in hypermobile joints.

The hypermobility syndrome describes hypermobile individuals with musculoskeletal complaints who lack the stigmata of other hereditary connective tissue disorders (Kirk et al., 1967). Wood (1971) suggested that these individuals simply represent one extreme in a normal variation of joint mobility throughout the population. Hypermobility can cause knee effusions (Sutro, 1947) and an association with many orthopaedic complaints has been described including dislocation of the hips (Carter and Wilkinson, 1964). Although the early rheumatic manifestations of hypermobility are well documented there is less information on the late natural history of these individuals. An association with premature osteoarthrosis has been described (Rowatt-Brown and Rose, 1966; Rotés Querol, 1971) and Kirk et al. found degenerative joint disease in 5 adult females out of their 24 cases. The only published report of synovial histology is a single needle biopsy of synovium from an adolescent with knee effusions that showed no serious inflammation (Ansell, 1972). We therefore decided to review 21 adult patients with generalised hypermobility who have presented to this hospital with rheumatic complaints over the past 2 years and, where possible to obtain synovial histology.

Patients and methods

Twenty-one patients were considered to have generalised joint hypermobility on first attendance. All were recalled for further interview by one of us (H.A.B.) and hypermobility was assessed by the method of Beighton et al. (1973) modified from Carter and Wilkinson (1964). Patients were thus given a numerical score of 0 to 9, one point being allocated for the ability to perform each of the following tests. (1) Passive dorsiflexion of the little fingers beyond 90°. (2) Passive opposition of the thumbs to the flexor aspects of the forearms. (3) Hyperextension of the elbows beyond 10°. (4) Hyperextension of the knees beyond 10°. (5) Forward flexion of the trunk with knees extended so that the palms of the hands rested on the floor.

A full clinical and family history was taken in each case and the details of patients are given in Table 1. Full blood count, plasma viscosity, and Rose-Waaler tests were performed on all patients and other investigations done as indicated. X-rays of the knees and of any painful joints were taken on each patient.

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Eight patients had synovitis with effusion in the knee joint. 7 of these agreed to arthroscopy which was done under local anaesthetic with a Storz instrument and routine biopsies and photographs were taken. In 3 patients additional surgical biopsy material was available (Table 2).

An age- and sex-matched group of 21 non-hypermobile patients also referred to a rheumatology clinic with musculoskeletal complaints were chosen at random and investigated as above. None had a hypermobility score of more than 1.7 age- and sex-matched nonhypermobile patients attending for diagnostic arthroscopy for persistent knee effusion completed the control group.

Results

HISTORY

All patients presented with musculoskeletal symptoms. Most gave a past history of such complaints,

Table 1  Details of 21 patients

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Hypermobility score (figures in brackets represent score in youth)</th>
<th>Dislocations</th>
<th>Other pathology</th>
<th>Radiological evidence of osteoarthrosis</th>
<th>Viscosity</th>
<th>Rose-Waaler</th>
<th>Arthroscopy</th>
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<td>1</td>
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<td>F</td>
<td>6</td>
<td></td>
<td></td>
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<td>-ve</td>
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<td></td>
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<td></td>
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<tr>
<td>3</td>
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<td>F</td>
<td>6</td>
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<td></td>
</tr>
<tr>
<td>4</td>
<td>42</td>
<td>F</td>
<td>8</td>
<td></td>
<td></td>
<td>Patella</td>
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<td>-ve</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>80</td>
<td>F</td>
<td>8</td>
<td></td>
<td></td>
<td>Knees</td>
<td>1.62</td>
<td>-ve</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>64</td>
<td>F</td>
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<td></td>
<td>Knees</td>
<td>1.70</td>
<td>-ve</td>
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<td></td>
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<td>-ve</td>
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<tr>
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<td>Myxoedema</td>
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<td>-ve</td>
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<td></td>
<td></td>
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<td>-ve</td>
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<tr>
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<td>2 (6)</td>
<td>Both hips</td>
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<td>Cervical spine/</td>
<td>1.69</td>
<td>-ve</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>66</td>
<td>F</td>
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<td>thumb base/</td>
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<td>61</td>
<td>F</td>
<td>5</td>
<td></td>
<td></td>
<td>Knees/sknee</td>
<td>1.59</td>
<td>-ve</td>
<td></td>
</tr>
<tr>
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<td>50</td>
<td>F</td>
<td>2 (7)</td>
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<td></td>
<td>Hips/sknee</td>
<td>1.58</td>
<td>-ve</td>
<td></td>
</tr>
<tr>
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<td>75</td>
<td>F</td>
<td>4 (6)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
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<td>70</td>
<td>F</td>
<td>6</td>
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<td></td>
<td>2.28</td>
<td>+ve</td>
<td>Yes</td>
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<td>18</td>
<td>65</td>
<td>F</td>
<td>6</td>
<td>Rheumatoid arthritis</td>
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<td></td>
<td>1.99</td>
<td>+ve</td>
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<tr>
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<td>44</td>
<td>M</td>
<td>4</td>
<td>Psoriatic arthritis</td>
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<td></td>
<td>1.78</td>
<td>-ve</td>
<td></td>
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<tr>
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<td>54</td>
<td>F</td>
<td>9</td>
<td>Raised immuno-</td>
<td>Rheumatoid arthritis</td>
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<td>2.20</td>
<td>+ve</td>
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<tr>
<td>21</td>
<td>48</td>
<td>F</td>
<td>4</td>
<td>Thumb base</td>
<td></td>
<td></td>
<td>1.82</td>
<td>+ve</td>
<td></td>
</tr>
</tbody>
</table>

Table 2  Arthroscopy and histology findings

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Age (years)</th>
<th>Viscosity</th>
<th>Arthroscopy findings</th>
<th>Histology*</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>43</td>
<td>1.61</td>
<td>Thickened synovium, mild osteoarthrosis, no crystals</td>
<td>No biopsy taken</td>
</tr>
<tr>
<td>15</td>
<td>50</td>
<td>1.59</td>
<td>Synovial proliferation; minimal osteoarthrosis, no crystals</td>
<td>No abnormality seen</td>
</tr>
<tr>
<td>13</td>
<td>66</td>
<td>1.69</td>
<td>Osteoarthrosis, chondrocalcinosis, bleeding tendency</td>
<td>Severe chondrocalcinosis; wrist synovectomy; proliferation of lining membrane with marked iron deposition; no inflammatory response</td>
</tr>
<tr>
<td>14</td>
<td>61</td>
<td>1.62</td>
<td>Osteoarthrosis, chondrocalcinosis</td>
<td>Osteoarthrosis and chondrocalcinosis</td>
</tr>
<tr>
<td>16</td>
<td>75</td>
<td>1.58</td>
<td>Osteoarthrosis, chondrocalcinosis</td>
<td>Changes suggestive of chondrocalcinosis</td>
</tr>
<tr>
<td>12</td>
<td>60</td>
<td>1.50</td>
<td>Calcified capsule, severe osteoarthrosis, chondrocalcinosis</td>
<td>Osteoarthrosis and chondrocalcinosis</td>
</tr>
<tr>
<td>10</td>
<td>70</td>
<td>1.58</td>
<td>Not done</td>
<td>Shoulder synovectomy; osteoarthrosis and changes suggestive of chondrocalcinosis</td>
</tr>
<tr>
<td>17</td>
<td>70</td>
<td>2.28</td>
<td>Vascular synovium, inflammatory arthritis, fibrin, no crystals</td>
<td>Changes consistent with psoriatic arthritis</td>
</tr>
</tbody>
</table>

*Findings in biopsies taken at knee arthroscopies unless stated otherwise.
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including muscle cramps aggravated by moving joints to extremes of their range, 'growing pains', spontaneous joint effusions, ease of dislocation, and in 3 patients a symptom complex resembling Raynaud's phenomenon. There was a higher incidence of easy bruising, poor healing of the skin, and varicose veins than in the control group. Patients also described symptoms attributable to secondary osteoarthritis and several of the older patients described intermittent symptoms typical of chondrocalcinosis especially in their most mobile joints. All patients except one were female. The symptoms increased with age and there was an impression of rapid deterioration in the fourth or fifth decade. 3 patients had a history of spontaneous tendon rupture. Half the patients considered themselves double-jointed though most agreed that joint laxity had decreased with age. The 5 patients with a raised PV described the above features in addition to symptoms attributable to their concomitant disease.

FAMILY HISTORY
This was only accepted where the history of joint hypermobility and osteoarthritis could be confirmed by hospital notes, practitioners' records, or examination of relatives. Although most patients claimed to have relatives with 'loose joints', or 'arthritis', careful checking validated only 9 histories. One of these families had hypermobility without osteoarthritis but in the other 8, osteoarthritis was seen in hypermobile patients. Two families had more than one member with seropositive rheumatoid arthritis.

EXAMINATION
Although patients with a hypermobility score of less than 4 were excluded from the study, these scores (Table 1) fall with age and 3 patients with a score of less than 4 were admitted to the study when a higher score in youth could be accurately confirmed. Additional diagnoses confirmed by the appropriate investigations are shown in Table 1 along with sites of dislocation and radiological distribution of osteoarthritis.

Synovial thickening, often bilateral and mainly in the more hypermobile joints, was observed in most patients. Occasionally there was abnormal skin laxity and a tendency to bruising. Tendon imbalance across lax peripheral joints caused swan neck deformity in 2 patients in the absence of demonstrable rheumatoid arthritis. 3 patients later reattended with transient acute monarthritis resembling crystal deposition disease at the thumb base. None of these findings, all considered typical of hypermobility, was seen in the control group.

PLASMA VISCOSITY
This was normal in 16 patients and abnormal in 5. This test formed the basis for distinguishing those patients with hypermobility arthritis alone from patients with a further pathology. Investigation showed the following diagnoses in patients with a raised viscosity: 2 with classical rheumatoid arthritis (ARA criteria), 1 rheumatoid arthritis with psoriasis, 1 psoriatic arthropathy, 1 suspected myeloma. A further patient (Case 9) had a suspected connective tissue disorder with vasculitis in spite of a normal PV.

RADIOLOGY
Osteoarthritis was found at the sites indicated in Table 1. In general the older the patient the worse the radiological appearances. In several patients there was a progression over 20 years from mild radiological appearances with osteosclerosis, loss of joint cartilage, and osteophytes to a bizarre appearance with extensive calcification more typical of a Charcot joint (Figs. 1 and 2). No patient with a normal PV had erosions or any radiological features of rheumatoid arthritis. However, in patients with a raised PV radiological changes of rheumatoid arthritis were superimposed on the osteoarthrotic pattern of their hypermobile joints.

Examination of X-rays in the nonhypermobile control group showed only 2 patients with radiological evidence of polyarticular osteoarthritis comparable in severity to that seen in the hypermobile group. There was a clinical impression that the onset of osteoarthritis was earlier in hypermobile patients but it was not possible to make an exact age comparison in this retrospective study.

Synovial thickening, presumed traumatic, was extensive in many hypermobile patients and Fig. 3 shows a synoviogram of the wrist in a patient where rheumatoid arthritis could not be shown.

ARTHROSCOPY
Seven patients (Table 1) agreed to arthroscopy of the knee. 6 were from the normal PV group and 1 from the raised PV group. Biopsies were taken in 6 of these patients and arthroscopy findings are compared with the histological findings in Table 2 in which details of further available biopsy material is also given. Arthroscopic appearances in the 2 patients with the least severe radiological change (Cases 11, 15) were identical. There was thickened synovium with no increased vascularity, no crystals, and no bleeding tendency. There were minimal osteoarthrotic changes and bone surfaces looked almost normal. 3 patients with more severe clinical and radiological change (Cases 13, 14, 16) had all the above changes but more severe osteoarthrosis and crystals of chondrocalcinosis.
Arthroscopy and histology subsequently confirmed chondrocalcinosis. X-rays had been abnormal for 5 years.

Fig. 1  Case 14, aged 61. 

Fig. 2  Case 12, aged 60. 
X-rays had shown progressive deterioration over 15 years. Arthroscopy confirmed chondrocalcinosis.
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Fig. 3 Case 12. Wrist synoviogram showing extent of synovitis in the absence of demonstrable rheumatoid arthritis.

Fig. 4

Figs. 4, 5, 6 Case 13. Arthroscopic appearances include a proliferative but relatively avascular synovium and fine avascular villi, both with crystals. Examination under a polarising microscope of crystals removed under direct vision confirmed chondrocalcinosis.

in each case (Figs. 4, 5, 6). These crystals had not been apparent either on x-ray or on examination of aspirated joint fluid. A sixth patient (Case 12) had the most severe change and arthroscopy was technically unsatisfactory because of a calcified capsule and gross joint destruction though chondrocalcinosis was seen. However, biopsy from a previous arthroscopy was available.

Fig. 5
The single patient arthroscoped from the raised PV group (Case 17) had completely different synovial appearances. The vascular synovium with broad based villi, fibrin formation, and absence of crystals were in keeping with the clinical diagnosis of psoriatic arthritis appearing in a hypermobile joint and histology confirmed this.

**PATHOLOGY**

Synovial biopsies from the knee joints of 6 patients were taken at arthroscopy. A wrist synovectomy specimen was available from one of these (Case 13) and a further patient (Case 10) had had a shoulder joint synovectomy for symptoms resembling polymyalgia rheumatica. In retrospect these may have been attributed to hypermobility.

Three biopsies showed changes characteristic of chondrocalcinosis. In one (Case 13) the changes were very florid with the villi virtually replaced by rounded masses of crystalline material which in areas provoked a low grade foreign body giant cell reaction (Fig. 7). The other two biopsies (Cases 12, 14) showed smaller masses of crystalline material lying within, or just below, the synovial lining (Fig. 8). A further biopsy (Case 16) and the shoulder synovectomy specimen (Case 10) showed suggestive but not diagnostic changes of chondrocalcinosis. Most of the biopsies showed some degree of lining membrane hyperplasia up to three cells wide and in the wrist synovectomy specimen from Case 13 this was prominent with...
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marked iron deposition consistent with traumatic synovitis. This may be attributed to a bleeding tendency more marked at arthroscopy in this patient than in any other. The remaining two biopsies showed no evidence of crystal deposition but one (Case 17) had changes consistent with the diagnosis of psoriatic arthritis (Table 2).

Inflammatory changes were virtually absent from all these specimens and the histological changes mirrored the arthroscopy findings confirming the presence of chondrocalcinosis in the 4 cases where it was visualised. In 7 age- and sex-matched non-hypermobile patients with a joint score of less than 1, referred for diagnostic arthroscopy, no examples of chondrocalcinosis were seen or found on histology.

Discussion

Hypermobility represents one extreme of a normal variation in joint mobility throughout the population (Wood, 1971; Beighton et al., 1973) and may prove advantageous in some professions (Grahame and Jenkins, 1972). There is also some evidence of a distinct autosomal dominant inheritance (Beighton and Horan, 1970) though these patients may be spared premature osteoarthrosis. Ethnic differences have been noted (Schweitzer, 1970) and hypermobility also varies with age, sex, and athletic training. All this leads to difficulty in defining hypermobility and the criteria generally used take no account of the reduction in mobility with age and the even greater reduction that can occur when osteoarthrosis develops. We defined generalised hypermobility as a score of 4 or more, but this is an arbitrary level. We preferred a simple scoring system in conjunction with a careful clinical history to some of the more complex scoring systems that are said to cover all these variations.

Superimposed on this range of joint mobility are specific inherited disorders of connective tissue. We have attempted to exclude such patients from this study but the division is not always distinct. Thus although the benign hypermobile variant of Ehlers-Danlos syndrome is said to be distinguished from
joint hypermobility by abnormal healing of the skin, we have found that this distinction is hard to make in practice. It is possible our series includes some mild examples of this syndrome and we have been impressed by the frequency of varicose veins and easy bruising in many of our patients. Whatever the genetic inheritance, we suspect joint hypermobility is part of a more generalised connective tissue disorder that involves all parts of the body. An elastic joint capsule can only be used if there is play in the skin, blood vessels, and ligaments along with adequate muscle relaxation.

Hypermobile patients are as susceptible as any to the whole spectrum of rheumatic disease. We have used the plasma viscosity in conjunction with a careful clinical history to distinguish the patients who developed a new disease late in life in their hypermobile joints from those with a gradual progressive history who might be considered to display the late results of possessing hypermobile joints.

It has not been possible to assess the prevalence of osteoarthrosis and hypermobility in a small study of this kind. Patients are already preselected by their attendance at hospital and this may account for the impression sometimes claimed that hypermobility is more frequent in the higher social classes. It is also hard to quantify osteoarthrosis. We have simply reinforced the strong clinical impression that hypermobile joints are associated with premature polyarticular osteoarthrosis.

The association of chondrocalcinosis and hypermobility has not previously been recorded. No examples were seen in the matched nonhypermobility arthroscopy group and in the last 50 arthroscopies performed at this hospital chondrocalcinosis has been diagnosed seven times, four of these in hypermobile patients. We have been impressed with the arthroscope as a method of demonstrating chondrocalcinosis when it was not detectable radiologically and when joint aspiration had failed to show crystals. Synovial biopsy under direct vision at arthroscopy with immediate polarising microscopy may be the method of choice for diagnosing chondrocalcinosis.

The initial symptomatology of hypermobility has been described (Kirk et al., 1967). It is suggested that the subsequent natural history of hypermobility leads to traumatic synovitis and later to osteoarthrosis, normally in the fourth or fifth decades. Chondrocalcinosis appears about 10 years later and the final stage in the progression almost resembles a Charcot joint with gross deforming osteoarthrosis, chondrocalcinosis, and a tough calcified synovium. We believe this progression deserves better recognition as ‘the arthritis of hypermobility’.

Many of our late x-rays from hypermobile patients show changes similar to those seen in the premature osteoarthrosis of ochronosis (Schumacher and Holdsworth, 1977). If hypermobility is accepted as a hereditary variant in the structure of connective tissue there is a common link between these disorders since in both the joints are subjected to an abnormal biochemical environment throughout life. McCarty (1977) has suggested that chondrocalcinosis may be the final end point of all such hereditary disorders and our findings support this view. It is possible that chondrocalcinosis would be found in all late cases of hypermobility in which it was looked for and further studies are required using the arthroscope as a means of detecting previously unsuspected chondrocalcinosis. It is even possible that chondrocalcinosis is the end point of all osteoarthrosis but only individuals with abnormal joint biochemistry and therefore premature osteoarthrosis see it within their lifetime.

Rheumatoid arthritis may develop in hypermobile patients and Ansell (1972) described such a case. 3 patients in our series of 21 fit this diagnosis. In one (Case 17) inflammatory arthritis with abundant fibrin was confirmed at arthroscopy and in another there was clear radiological evidence of rheumatoid arthritis and osteoarthrosis coexisting. Such patients must be distinguished from those with rheumatoid arthritis who may have acquired hypermobility by regular exercise. Thus patients with fixed deformities at the ankles and knees find it advantageous to develop abnormally good hip flexion in order to put on shoes. It remains uncertain whether this is purely an acquired hypermobility or whether they have hereditary hypermobility before the onset of disease.

We also suggest that the later consequences of hypermobility can easily mimic rheumatoid arthritis. Dorwart and Schumacher (1974) drew attention to hypermobile hands that resembled rheumatoid arthritis and several of our patients were initially referred with this erroneous diagnosis. They had bilateral synovial thickening, presumed traumatic, tending to involve the most mobile joints. The fingers could sometimes be placed into a swan neck position because of ligamentous laxity and spontaneous tendon rupture can occur in these patients in the presence of a thickened synovium. Osteoarthrosis causes joint pain and when chondrocalcinosis appears the joints become hot as well as swollen. Although rheumatoid arthritis may be suspected, it can usually be excluded by a normal PV, absence of radiological erosions, and the standard serological tests for rheumatoid remaining negative.

We thank Dr J. A. Cosh and Dr A. St. J. Dixon for permission to report their patients, and Miss E. F. Lupton for secretarial help.
References


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