Another look at osteoarthritis*

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SUMMARY One hundred consecutive cases of osteoarthritis seen in a medical clinic have been reviewed and contrasted with 100 patients with rheumatoid disease. Osteoarthritis was usually a polyarticular disease and as symmetrical in distribution as rheumatoid; the knees and hands were the most commonly involved sites. Evidence of inflammation was often found in patients with osteoarthritis and included morning stiffness, redness of distal interphalangeal joints, warmth, and effusions in the knees. In many cases there was either radiological or electron microscopical evidence of deposition of calcium salts. These findings do not support the concept of osteoarthritis as a mechanical, noninflammatory 'wear and tear' condition. An active metabolic abnormality of articular cartilage resulting in cartilage destruction, calcification, and inflammation is suggested as being more compatible with the findings.

Osteoarthritis is traditionally viewed as an aging process of cartilage, related to wear and tear and therefore occurring predominantly in weight-bearing joints. An extension of this theory postulates that unprotected load bearing damages chondrocytes and leads to release of enzymes which degrade cartilage (Radin, 1976). This concept is well described by the term 'degenerative joint disease'. Because the disease is seen as a purely meachanical condition devoid of inflammation the term 'osteoarthrosis' is preferred by some authors.

It is already clear that this concept is inappropriate in some types of disease such as primary generalised osteoarthritis (Kellgren and Moore, 1952), inflammatory osteoarthritis (Ehrlich, 1975), and erosive osteoarthritis (Peter *et al.*, 1966). These have been regarded as variants of the disease. But there is evidence, both morphological (Sokoloff, in press) and biochemical (Muir, 1977), that cartilage changes in osteoarthritis differ from those of the aging process.

There is also evidence that osteoarthritis may be associated with deposition of crystals of calcium pyrophosphate dihydrate (McCarty, 1975). The recent discovery of crystals of hydroxyapatite in some cases of osteoarthritis (Dieppe *et al.*, 1976) suggested the need for a reappraisal of the clinical and radiological features of the disease.

Patients and methods

One hundred consecutive patients seen in a specialist rheumatology clinic by 2 physicians and diagnosed on the basis of clinical and radiological features as suffering from osteoarthritis were studied. The diagnosis was based on clinical features supported by the radiological criteria of Kellgren and Lawrence (1957). A control group of 100 consecutive cases of rheumatoid arthritis, definite or classical by American Rheumatism Association (ARA) criteria, was used for comparison.

Age, sex, and duration of disease were noted. Pain severity was recorded on a visual analogue scale. The patients were asked to complete a daily record, measuring pain severity every 2 hours on a visual analogue scale to determine the diurnal pattern of pain. Each patient was asked whether he was stiff on waking in the morning and after sitting and, if so, to estimate the duration of stiffness in minutes.

A careful history was taken in each case to determine the joint which was first affected and the subsequent pattern of development of the illness. The date of onset and severity of all affected joints were noted. All joints were examined and abnormal findings noted. Involvement was expressed in terms of both individual joints and sites such as hands, wrists, or knees.

A family history was obtained and any possible predisposing factors in the past medical history were noted.

X-rays were taken of the hands, knees, hips, and dorsal spine in all cases and of other affected joints if necessary to establish the diagnosis. The films were

examined by 2 radiologists, who documented the classical radiological signs of osteoarthritis (loss of joint space, sclerosis, subchondral cysts, and osteophytes), the presence of other signs such as erosions or joint destruction which might suggest an alternative diagnosis, chondrocalcinosis articularis, and ankylosing vertebral hyperostosis. The number, size, and site of any radio-opaque bodies and the presence or absence of trabeculation within them was noted.

Blood was taken for erythrocyte sedimentation rate (ESR), latex test, and estimation of calcium, phosphates, and alkaline phosphatase.

Synovial fluid was available for analysis in 34 cases. The appearance of the fluid was noted and a total and differential white cell count performed. A search for crystals was made by conventional polarised light microscopy and also by the technique of transmission and scanning electron microscopy combined with energy dispersive microanalysis (Crocker *et al.*, 1976).

A control group of 100 patients with a clinical diagnosis of rheumatoid arthritis was also studied. Measurements included pain severity, the duration of morning and inactivity stiffness, ESR, latex test, calcium, phosphates, and alkaline phosphatase. Age, sex, and duration of disease were noted along with the pattern of development of the arthritis and joints affected by it. *X*-rays of the hands were examined.

The statistical significance of differences between measurements made in the 2 groups of patients was assessed by Student's *t* test. The chi-squared test was applied to the frequency of various occurrences such as involvement of a particular joint in the two groups.

Results

The means of some clinical and laboratory findings are summarised in Table 1.

Table 1 *Means of some clinical and laboratory findings in patients with osteoarthritis and rheumatoid arthritis*

Measurement	Osteoarthritis	Rheumatoid arthritis
Age (at survey)	60·3	52·3
Age (at onset)	50·6	39·8
Sex (F:M ratio)	7:3	7:2
Pain severity	10·6	10·5
Duration of morning stiffness (minutes)	22·5	58·2
Duration of inactivity stiffness (minutes)	8·0	7·1
ESR (mm at 1 hour)	14·3	54·6
Latex test (% positive)	6	81
Calcium (mmol/l)	2·41	2·31
Corrected calcium (mmol/l)	2·59	2·55
Phosphates (mmol/l)	1·14	1·20
Alkaline phosphatase (international units)	67·3	100·4

CLINICAL FINDINGS

Most cases of osteoarthritis began between the ages of 35 and 70 with a peak between 45 and 55. It was a little more than twice as common in women than men. Rheumatoid patients were a little younger and their disease had started on average about 10 years earlier, with a peak between 35 and 45.

The severity of pain measured on a visual analogue scale was almost identical in patients with rheumatoid and osteoarthritis. The diurnal pattern of pain in osteoarthritis is shown in Fig. 1. Pain was worst at the end of the day with a smaller morning rise. In many patients there were exacerbations during the day related to particular activities.

The duration of morning stiffness in rheumatoid and osteoarthritis is shown in Fig. 2. 83% of patients with osteoarthritis had some morning stiffness compared to 92% of patients with rheumatoid arthritis, but it was significantly briefer. It was localised to 1 site in 55% of the 83 patients who had it and to more than 2 sites in only 10%. Morning stiffness confined to both knees was the commonest symptom (34%). In rheumatoid arthritis morning stiffness was typically more widespread.

Inactivity stiffness was present in 83% of patients with osteoarthritis. The commonest duration was 5 minutes, and it seldom lasted more than 30 minutes. 87% of patients with rheumatoid arthritis had stiffness after sitting, and the mean duration was similar.

Only 2 cases of osteoarthritis had involvement of a single joint, a shoulder in one and a knee in another. The distribution of affected joints is shown in Fig. 3 and 4. Most patients had 1, 2, 3, or 4 sites of disease.
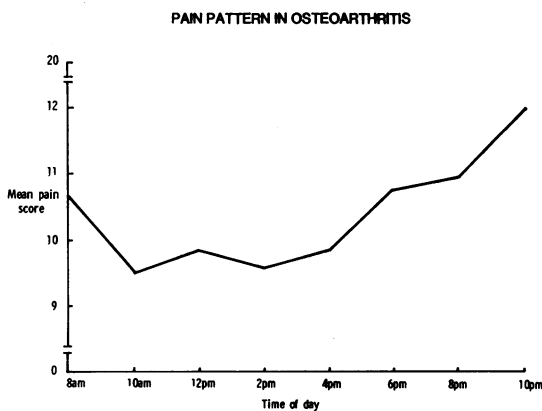

Fig. 1 *Pain pattern in osteoarthritis, based on measurement with a visual analogue scale every 2 hours throughout the day.*
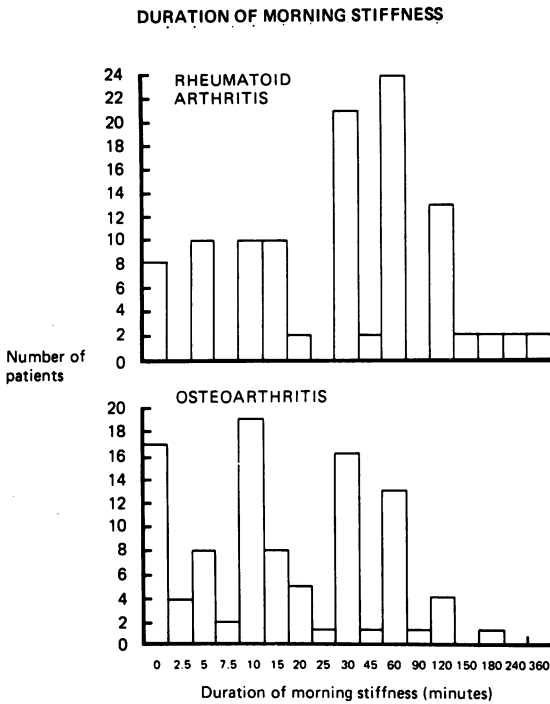
DURATION OF MORNING STIFFNESS

Fig. 2 *Duration of morning stiffness in patients with osteoarthritis compared to those with rheumatoid arthritis.*
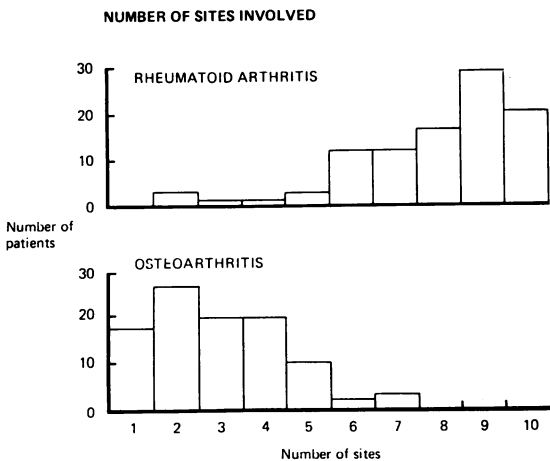
NUMBER OF SITES INVOLVED

Fig. 3 *Number of sites involved in patients with osteoarthritis and rheumatoid arthritis.*

The knee was the commonest site (75%), followed by the hands (60%). In the hands the commonest pattern of involvement was distal interphalangeal joints only or distal interphalangeal joints and first
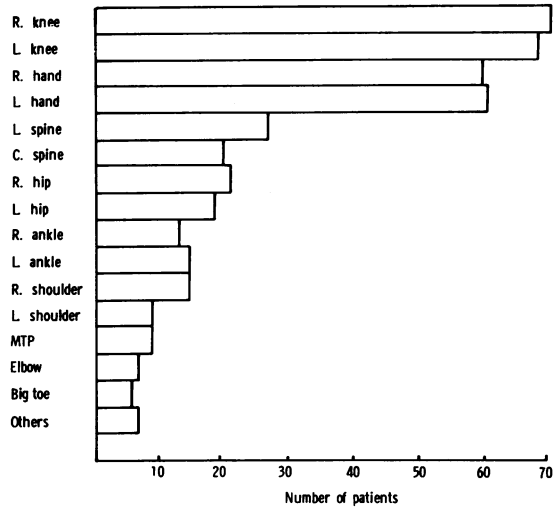

Fig. 4 *Joints affected in 100 patients with osteoarthritis.*

carpometacarpal joint (Table 2). No patients with rheumatoid arthritis had monarticular disease and most had 6 to 10 sites of disease.

The commonest presenting joints in patients with osteoarthritis were the knees (46%) and the hands (14%). In rheumatoid arthritis the commonest presenting joints were the hands (39%), feet (17%), knees (15%), and shoulders (12%). Osteoarthritis spread more slowly than rheumatoid, the mean delay between involvement of the first and second sites being 11 months in rheumatoid arthritis and 48 months in osteoarthritis.

A more detailed analysis of knee involvement was made to examine such factors as the effect of dominance and symmetry. Of the 74 patients with osteoarthritis involving the knees 63 (85%) had bilateral involvement. When only one knee was involved it was almost twice as often the right. In 51 cases (69%) the 2 knees were equally severe, but when one was worse it was again twice as often the right. Onset was simultaneous in 41 cases (65%) but when one began first it was twice as often the right.

Table 2 *Patterns of hand involvement (DIP=distal interphalangeal joints. PIP=proximal interphalangeal joints. MCP=metacarpo phalangeal joints. CMC= carpometacarpal joint of the thumb)*

DIP only	22	DIP + PIP + CMC	5
DIP + CMC	20	CMC only	4
DIP + PIP	8	MCP only	1*

*3 patients had MCP joint involvement in addition to other joints. No patient had involvement of PIP joints only.

In the 22 patients in whom one knee started before the other, the mean interval was 61·9 months; this varied from 1 month to 26 years.

Of the patients with rheumatoid arthritis 95% had knee lesions, and the symmetry was similar to that of osteoarthritis. The disease was bilateral in 91% and of equal severity in 64%. When one knee was worse or when one started before the other, it was almost twice as often the right as the left. Spread from one knee to the other was more rapid in rheumatoid arthritis, with a mean interval of 16·5 months in the 57 patients in whom the knees were not simultaneously affected.

Twenty-five patients mentioned some predisposing cause for their osteoarthritis, usually either trauma or sport. In most of these patients the disease was more widespread than could be explained by the injuries sustained.

Examination of the joints revealed signs of inflammation in many cases of osteoarthritis. Of the 74 patients with knee involvement 54 (73%) had effusions. In 19 (26%) one or other knee was noted to be warm, and in 31 (42%) a Baker's cyst was present. Redness of distal interphalangeal joints was noted in 10 cases (18% of those with involvement of this joint). Duration of disease did not differ significantly in patients with or without effusions in the knees or redness of distal interphalangeal joints.

RADIOLOGICAL FINDINGS

X-rays were available for study in 98 patients with osteoarthritis. Radiological evidence of osteoarthritis was present in all cases. The knees (61%) and hands (66%) were again the commonest sites, and only 9 patients did not have some changes at either of these sites. Hips were involved in 47 cases. Ankylosing vertebral hyperostosis was noted in 43. Chondrocalcinosis articularis (linear calcification of cartilage) was found in the knees in 5 cases. An entirely different pattern of calcification was seen more commonly. Opacities of calcific density were noted in the hands or knees in 72 cases, 60 in the hands and 27 in the knees. eight patients had similar calcification in the hips, and it was occasionally noted at other sites.

Calcific deposits in the hands were most commonly seen in the distal interphalangeal joints, with the index finger most often affected. Their characteristics are summarised in Table. 3 They were often multiple, small, and not usually trabeculated. By contrast, calcific deposits in the knees were larger and often trabeculated.

Confirmation of the nature of these deposits was possible in 5 cases, 4 requiring knee surgery and one who came to necropsy. In all these cases the deposits were attached to or embedded within soft tissue, and

Table 3 *Features of deposits of calcific density seen in x-rays of the hands and knees in 98 patients with osteoarthritis*

	Distal interphalangeal joints	Knees
Number of patients	55	27
Number of joints affected per patient (mean and range)	3·7 (1–8)	—
Number of deposits per joint (mean and range)	1·6 (1–10)	3·0 (1–8)
Size of deposits (in mm, mean and range)	1·6 (1–5)	5·4 (1–20)
Trabeculation present (%)	11	50

none were 'loose' bodies. Histologically 3 had a typical bony structure, but 3 lacked any trabeculation. Infrared spectrophotometry confirmed that hydroxyapatite was the dominant mineral in all cases.

There was a significant correlation between the presence of calcific deposits in the knees and clinical involvement. ($\chi^2 = 5·35$, P<0·05), but no such relationship existed for the hands. There was also a significant correlation between the presence of calcific deposits in the knees and the finding of a Baker's cyst. Patients with calcific deposits in the knees were no more likely to have effusions, warm joints, or hand involvement.

Opacities were found in the distal interphalangeal joint of 10 patients with rheumatoid arthritis.

LABORATORY FINDINGS

The ESR was more often normal and the latex test more often negative in patients with osteoarthritis than in those with rheumatoid arthritis (Table 1). The latex test was positive in 6% of patients with osteoarthritis, all at a low titre. Calcium and phosphate levels were normal in all patients with osteoarthritis.

However, serum calcium levels were significantly higher in patients with osteoarthritis than in those with rheumatoid arthritis whether or not they were corrected for differences in serum albumin. Alkaline phosphatase levels were slightly elevated in 6 patients with osteoarthritis and above the upper limit of normal (100 international units) in 28 patients with rheumatoid arthritis.

Synovial fluid was aspirated from the knee in 34 cases of osteoarthritis. The mean cell count was $3·45 \times 10^9$/cells/dl (0·3 to 15). Most effusions contained predominantly mononuclear cells (mean 80%). Polarised light microscopy revealed the presence of pyrophosphate crystals in 6 cases. Analytical electron microscopy revealed pyrophosphate in 7 cases and clumps of hydroxyapatite crystals in 9 cases. Two of the cases with hydroxyapatite crystals also had pyrophosphate in

Table 4 *Relationship between the pattern of radiological calcification and the nature of crystals found in synovial fluid*

	Radiological calcification		
Crystals in synovial fluid	None	'Spotty'	Linear
Hydroxyapatite	2	7	1
Pyrophosphate	2	1	4

the same fluid sample. Four of the 7 patients with pyrophoshate crystals had radiological evidence of chondrocalcinosis, and 7 of the 9 with hydroxyapatite had calcific deposits on *x*-ray (Table 4). Synovial fluid of 34 patients with rheumatoid arthritis was examined. The mean cell count was $14 \cdot 6 \times 10^9$ cells/dl ($0 \cdot 9$ to $55 \cdot 7$). Most effusions contained mainly polymorphs (mean 69%). No crystals were found in 15 cases examined by electron microscopy.

Discussion

The picture of osteoarthritis obtained in this survey was not in keeping with the idea of a non-inflammatory mechanical condition. The disease predominantly affected middle-aged women and was almost always polyarticular. The knees were the most frequently affected joint and often the dominant source of symptoms, but the hands and other non-weight-bearing joints were also frequently involved, and severe hip disease was uncommon. These findings support the epidemiological evidence which suggests that hip disease may be a separate entity, not linked to polyarticular osteoarthritis (Wood, 1976). The findings are also in keeping with those of 2 previous surveys of patients with symptomatic osteoarthritis, in which monoarticular disease was rare and middle-aged women most often affected (Cecil and Archer, 1926; Kellgren and Moore, 1952).

Recognition of the inflammatory component of a disease must still depend on the cardinal signs, pain, heat, redness, and swelling. To these might be added stiffness, which is a prominent symptom of inflammatory arthropathies such as rheumatoid arthritis. All are to be found in patients with osteoarthritis.

Pain is as severe as in rheumatoid arthritis, and many patients had joints which were warm, red, or swollen. The absence of morning stiffness has often been suggested as a helpful diagnostic feature of osteoarthritis, but it was noted by almost as many of our patients with osteoarthritis as those with rheumatoid arthritis. Synovial fluid also provided evidence for a low-grade inflammation with greater than normal numbers of cells.

This survey could be criticised because patients with osteoarthritis attending a medical clinic may be unrepresentative of the disease. One might obtain different results in an orthopaedic clinic, in general practice, or in a population survey based on people with radiological changes. Our patients were also receiving a variety of treatments which must certainly have modified some aspects of their disease such as the duration of morning stiffness. However, untreated patients are nowadays rare and probably also unrepresentative. We compared 2 groups of patients in a medical clinic setting, and our conclusions must be drawn on this basis.

We identified a number of important differences between our 2 groups of patients which are relevant to a physician in a medical clinic who is trying to distinguish rheumatoid from osteoarthritis. Patients with rheumatoid arthritis were about 10 years younger at the onset of their disease and complained of morning stiffness, which was more prolonged. While the pain in rheumatoid arthritis is usually worst in the morning (Huskisson, 1975), that of osteoarthritis was worse in the evening. Patients with rheumatoid arthritis had more joints involved than those with osteoarthritis. Osteoarthritis presented more frequently in the knees, while rheumatoid arthritis presented more often in the hands. The distribution of joints involved within the hand was also different. While rheumatoid arthritis affects the proximal interphalangeal joints more commonly (Lewis-Faning, 1950), it is the distal interphalangeal joint which bear the brunt of oteoarthritis. Osteoarthritis spread from joint to joint more slowly than did rheumatoid. Radiological calcification in joints was common in osteoarthritis and rare in rheumatoid arthritis. The classical *x*-ray changes of the two diseases are, of course, quite different. In rheumatoid arthritis the ESR was more often raised, the latex test more often positive, and alkaline phosphatase levels more often raised than in osteoarthritis. Synovial fluid findings were distinguished from those of rheumatoid arthritis by a lower cell count, predominantly mononuclear infilitrate and crystals in some cases.

Sex incidence, pain severity, inactivity stiffness, and the symmetry of joint involvement were not helpful in distinguishing the diseases.

This study has provided additional evidence for the importance of mineral deposition in osteoarthritis. The association of deposition of calcium pyrophosphate dihydrate and osteoarthritis is well known (McCarty, 1975); there was evidence of pyrophosphate deposition in about 10% of cases. But radiological calcification was very common, and in most cases the appearance was quite different from the linear calcification of chondrocalcinosis. Mineral deposits were found most often in the distal

interphalangeal joints of the hands. Deposits in the knees were larger and more often trabeculated, but this could well be related to the different size of the joints. Biospy in such cases revealed that the mineral of these deposits was hydroxyapatite. Hydroxyapatite crystals were found more commonly in synovial fluid from patients with osteoarthritis than pyrophosphate.

In view of the known association of pyrophosphate deposition and osteoarthritis it is tempting to postulate the association of hydroxyapatite deposition and osteoarthritis. In support of this Ali and Wisby (1975) have shown that hydroxyapatite can be found in the mid-zone of osteoarthritic cartilage, in the region of chondrocytes and around the fissures. Crystals released from this site into synovial fluid could then be seeded in the capsule or synovium and eventually produce deposits. The presence of hydroxyapatite is an attractive mechanism for the inflammatory component of the disease, and such crystals have been shown to be capable of inducing experimental inflammation (Dieppe *et al.*, 1976). Their presence may play no part in the progressive loss of cartilage which characterises osteoarthritis but may nevertheless provide some clue to the underlying metabolic abnormalities of the disease.

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