

## Osteoarthritis Beginning With Inflammation Definitions and Correlations

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• **A syndrome of acute onset of inflammation over interphalangeal joints heralding deforming osteoarthritis may be intermediate between degenerative and rheumatoid joint diseases. The syndrome appears predominantly in women of menopausal age and is remarkably symmetrical. In a prospective study of 170 propoiti, later changes more characteristic of rheumatoid arthritis than of generalized or erosive osteoarthritis developed in 15.3%. (JAMA 232:157-159, 1975)**

VARIOUS recent observations of changes at the molecular, cellular, or tissue level delineate the process that ultimately leads to osteoarthritis. The chemical and physical alterations reflect repeated trauma of any degree, developmental factors, the action of proteolytic enzymes and superoxide radical<sup>1</sup> elaborated during inflammation from any cause, and the gamut of factors contributing to aging. While the late elaboration of growth hormones in acromegaly is clearly related to proliferative and degenerative changes at joints, the possible influence of other hormonal imbalances has only been inferred. Thus, the development of nodose deformities resulting from narrowing of joints and proliferative bone changes at their margins in women during the years surrounding menopause implies at least a contributory role for endocrine changes. In addition, a family history

of osteoarthritis is often obtainable, in which women are much more at risk, and at earlier ages, than men. While there may be common basic mechanisms underlying the development of so-called degenerative changes of joints, the modes of expression readily segregate into various clinical syndromes.

The majority of instances are provoked by exogenous or developmental stimuli, which afflict single joints or an anatomically related sequence of joints. The fact that the more generalized variety,<sup>2,3</sup> chiefly interphalangeal but with associated large-joint and spinal lesions, develops in close temporal relationship at a number of different sites suggests a response to exogenous stimuli. In most cases, the onset is insidious, and pain is minimal to absent, becoming noticeable only after trauma to a somewhat deranged joint.<sup>4</sup> In some instances, however, the onset is heralded by inflammation.<sup>5</sup> In the surrounding skin, the classic signs become apparent: redness, warmth, swelling, pain and tenderness, and dysfunction. According to Waxman

and Sledge,<sup>6</sup> the qualification that the inflammation afflicts the surrounding tissues is unnecessary, as they have accumulated biochemical data to prove inflammatory changes within the joints as well. Levels of lysosomal proteolytic enzymes in knee joints that are developing erosive osteoarthritis are intermediate between normal and those levels found in standard degenerative joint disease and rheumatoid arthritis. The term, "inflammatory osteoarthritis," thus serves as a label for those cases of generalized osteoarthritis that begin abruptly, have inflammatory components, and subside, with sequelae that constitute the classic changes of osteoarthritis. These are generally erosive, as in the syndrome described by Peter and co-workers,<sup>3</sup> but nonerosive and even ankylosing interphalangeal osteoarthritis may also result.<sup>7</sup>

### Interphalangeal Osteoarthritis

A correlative analysis of 170 patients (164 women, six men) who, during a five-year period, were first seen with acute onset of interphalangeal osteoarthritis suggests that the syndrome is remarkably symmetrical.<sup>7</sup> Each distal interphalangeal joint was involved in more than 70% of patients, as shown in Table 1. Each proximal interphalangeal joint was involved in approximately 50%. The interphalangeal and metacarpophalangeal joints of the thumb and the

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trapeziometacarpal joint were frequent sites of predilection, but, to a lesser extent, all metacarpophalangeal joints could participate in the syndrome. Significantly, the joints of the ulnar side of the wrist and carpus were universally spared. Elbows and shoulders remained uninvolved, while simultaneous involvement of knees, hips, and cervical spine was recorded.

#### Symmetricality

Coefficients of correlation (Pearson product moment R) were determined, and demonstrated an almost linear relationship in involvement of contiguous interphalangeal joints (Table 2). A similar linearity characterized the symmetricality of involvement, so that when a given joint was involved on one side, its counterpart was as likely to be involved (Table 3). There was not quite as much likelihood of concurrent osteoarthritis in joints more remote from each other (second and fourth or fifth distal interphalangeal joint), but the concurrence was still sufficient to be statistically significant. Of the distal joints, the fourth distal interphalangeal joint was, by a small margin, the least often involved. While the predilection for adjacent joints might speak in favor of trauma as an important causal factor, the symmetricality argues against such a relationship. A correlation with advancing age obtained to a significant degree only at the knees, suggesting the possibility that a causal relationship might be more apparent than real and that the concurrence is fortuitous (right, .49; left, .40).

#### Ancillary Data

The abnormalities in the laboratory profile reflected moderate inflammation. The erythrocyte sedimentation rate, a nonspecific acute-phase reactant, was below 40 mm/hr (Westergren) in 79% of patients, and greater than 40 mm/hr in only 21%. Latex fixation test for rheumatoid factor was either negative (96%) or weakly positive in undiagnostic titers of below 1:80 (4%).

When obtained, roentgenograms invariably reflected some degree of erosive changes, as well as narrowing of the joint and proliferative changes at the margins.

	Interphalangeal Joint Involvement on Each Digit, %				
	1	2	3	4	5
Distal interphalangeal					
Right	...	78	72	73	75
Left	...	83	75	72	79
Interphalangeal					
Right	35	...	...	...	...
Left	29	...	...	...	...
Proximal interphalangeal					
Right	...	51	49	52	52
Left	...	53	52	51	50
Metacarpophalangeal					
Right	24	11	6	2	2
Left	28	13	8	2	1
Carpometacarpal					
Right	36	...	...	...	...
Left	37	...	...	...	...

	Right				Left			
	2	3	4	5	2	3	4	5
Distal interphalangeal								
2	...	.71	.55	.50	...	.77	.73	.63
3	.71	...	.75	.50	.77	...	.75	.72
4	.55	.75	...	.65	.73	.75	...	.84
Proximal interphalangeal								
2	...	.75	.73	.75	...	.81	.76	.72
3	.75	...	.81	.72	.81	...	.72	.72
4	.73	.81	...	.81	.76	.72	...	.76

#### Clinical Features

In all cases, the initial attack was characterized by marked redness over the involved interphalangeal joint, and engorgement of the finger pads. Besides the pain at the involved joints, and stiffness after rest for limited periods (generally less than one-half hour) at involved joints only, patients also complained of annoying fullness and tingling in the finger tips that awakened them at night and could only be relieved by shaking and otherwise moving the hands or submerging them in hot water.

These symptoms were relatively self-limited, lasting from weeks to five years; they could be controlled with standard anti-inflammatory medications and the wearing of stretch gloves at night. Administration of female sex-hormone replacement therapy could prolong the symptoms or postpone them until ultimate withdrawal of hormone treat-

Right	Left					Knee	Hip
	1	2	3	4	5		
Distal interphalangeal							
2	.77						
3		.85					
4			.82				
5				.74			
Proximal interphalangeal							
2	.77						
3		.87					
4			.75				
5				.87			
Interphalangeal							
1	.75						
Metacarpophalangeal							
1	.82						
2		.92					
3			.91				
4				.57			
5					.81		
Carpometacarpal							
1	.71						
Knee						.80	
Hip							.59

ment. Despite symptomatic improvement, residual findings remained, most notably, nodose deformity of the previously inflamed joint and characteristic instability and malalignment of the finger joints (and knee joints as well). In five cases, interphalangeal joints ankylosed.

#### Superimposition of Rheumatoid Arthritis

It is important, however, that in 15.3% of the patients (25 women, one man), a second acute inflammatory episode occurred some time after the initial attack of osteoarthritis had subsided.<sup>9</sup> This second attack followed onset of the first by an average of 12 years (average age at onset of osteoarthritis, 51.5 years; of rheumatoid arthritis, 63.3 years), although the time after subsidence of initial symptoms before the second episode was considerably shorter. In all these patients, tenosynovitis of the extensor carpi ulnaris tendon at the wrist developed, and in 23 of the 26, tenosynovitis of the extensor digitorum communis at the wrist. Rheumatoid nodules formed at or near the elbow

in eight, and in tendons in three patients. Flexion contractures developed at the elbows in 22 patients; in 15, contractures were accompanied by synovitis. Morning stiffness, now generalized, became prolonged—one to five hours—and was more difficult to combat.

Erythrocyte sedimentation rate became more rapid, averaging 71 mm/hr (Westergren), and hemoglobin levels declined to less than 11.5 gm/100 ml in 17 patients. Latex fixation test became positive for rheumatoid factor in titers of 1:80 or higher in nine patients. Lupus erythematosus cells and antinuclear antibodies were not demonstrable, and complement levels remained within the normal range in the eight patients tested. Roentgenograms showed development of juxta-articular osteoporosis, soft-tissue swelling, and minor early rheumatoid changes of the wrists in all patients. More extensive changes—subluxations, dislocations, and joint destruction by pannus—developed in only four patients. Five patients underwent surgical correction of lesions; the resected tissue was characteristic

of rheumatoid arthritis.

Four of the five patients who had had ankylosis as an element in osteoarthritis are found in this group who fulfilled all criteria for definite rheumatoid arthritis.

The frequent occurrence of superimposition of a syndrome indistinguishable from rheumatoid arthritis on a chronic osteoarthritic condition that initially had inflammatory component is noteworthy, and should probably not be attributed solely to peculiarities of patient selection. Certainly, these patients represent a subgroup of the cases labeled by the more inclusive German term, "Propf-PCP" ("engrafted rheumatoid arthritis").<sup>10</sup> The possibility of generalization of an intra-articular process, characterized by an antigen-antibody reaction resulting from inflammation, cannot be dismissed. This inference would place inflammatory osteoarthritis at the interface between noninflammatory osteoarthritis and rheumatoid arthritis,<sup>11</sup> in conformity with the data of Waxman and Sledge,<sup>8</sup> with the exact role of endocrine causation still to be defined.

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