Cartilage metabolism—A response

On the basis of measurements of the concentration of aggrecan fragments, cartilage oligomeric matrix protein (COMP), normalized for dilation, and TIMP in samples of synovial fluid obtained from injured and uninjured knees of subjects with unilateral knee trauma, Dahlberg and colleagues concluded that an abnormality of cartilage metabolism existed in the contralateral knee and suggested that mechanical compensation for the injury, or cytokines or other products released from the injured joint initiated a pathological process in the uninjured knee.

The authors provided reference values for concentrations of the above molecules in a control group of 10 healthy athletes without knee symptoms and with no previous knee injury. However, the median volume of synovial fluid aspirated from the reference group (2-5 ml) was some 3-5 times greater than that from the uninjured knee of subjects with unilateral knee injury, strongly suggesting that the reference group was not normal. Unfortunately, results of routine synovial fluid analyses (total leukocyte count and differential) were not provided.

If concentrations of the various markers are normalized for volume, using the median synovial fluid volume in the uninjured knee of the subjects with unilateral injury (0.7-1.0 ml), the median quantity of aggrecan, for example, present in synovial fluid samples from the reference group was nearly 150% greater than that in samples from the contralateral knee of the subjects with knee injury, raising doubt about the authors’ interpretation of the findings for the contralateral knee.

Other factors may also have confounded the results. Did subjects limit usage of the injured joint as a result of pain? This would have decreased the rate of clearance of protein from the joint space. In contrast, synovial inflammation resulting from the injury would have increased clearance of the ‘marker’ from the joint space; even low grade synovitis with a synovial leukocyte count no greater than 1000-2000 cells/mm², may increase clearance of protein from the joint space three- to fourfold. If the rate of clearance is not controlled for, the authors concluded that abnormalities in synovial fluid concentrations of the molecules measured reflect quantitative changes in articular cartilage metabolism may be misleading. The possibility that joint structures other than articular cartilage (inflamed synovium, damaged cruciate ligament or meniscus) contributed significantly to the synovial fluid concentrations of the molecules measured should also not be overlooked.

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Autosomal dominant undifferentiated spondyloarthropathy not related to the HLA system

We were interested to read the article by Kidd and colleagues1 on familial aggregation for undifferentiated spondyloarthropathy associated with HLA-B7. The authors described a single family in whom numerous members had a non-pondenogamous arthropathy or enthesopathy, or both, which fulfilled the European Spondylarthropathy Study Group criteria for spondyloarthropathy2 in the absence of the HLA-B27 tissue type, coexistent psoriasis, or inflammatory bowel disease. They suggested that 'undifferentiated' spondyloarthropathy can be associated with genetic factors other than HLA-B27. We are in total agreement.

A few years ago, we studied a French family of 83 members distributed over five generations divided into four main branches, among whom 18 adult members had destructive arthropathy and enthesopathic changes.3,4 In all patients, the disease began between the ages of 18 and 32 years. It affected predominantly the wrists, fingers, shoulders, and peripheral entheses and progressed as an oligoarthritis, with intermittent inflammatory episodes lasting for one to three months. Axial involvement of the cervical and lumbar spine and the sacroiliac joints was also seen, but was not prominent. The sites of involvement seemed to be influenced by mechanical factors. The right wrist was generally the first joint to be affected. Destructive abnormalities, followed by bony proliferation, and intra- or extraarticular bony ankylosis were the main radiological features of this familial arthropathy (figure).

The transmission of the disease was dominant and autosomal, with 100% penetrance. The clinical and radiological features were strikingly similar in all patients and were suggestive of different generations and different branches of the genealogical tree, telling monogenic transmission. HLA typing of 12 patients and 13 healthy family members was performed. No HLA antigen was linked to the disease. None of the affected subjects had antigens B27, DR4 or DR7. The disease was not transmitted with any particular HLA haplotype.

Tests for rheumatoid factor yielded negative results. There was no history of psoriasis or chronic enteropathy in the members of this family. In none of the 18 patients did the arthropathy fulfil the American Rheumatism Association criteria.1 A diagnosis of ankylosing spondylitis was also eliminated, because the New York criteria were not fulfilled.2 This familial arthropathy could belong to the class of undifferentiated spondyloarthropathies proposed by Bucchini and Calif3. The spondyloarthropathies have in common a non-specific inflammation of the entheses, involving both the chondrified and the calcified parts. After a destructive phase, which causes bony erosion, repair takes the form of ossification.4,5 An inherited abnormality in the collagen matrix of the entheses may predispose to destructive arthropathy and enthesopathic changes. Linkage analysis of the COL2A1 as the disease causing locus in this family.6 Further studies are needed to identify the genetic locus responsible for the disease.

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doi: 10.1136/ard.54.8.685-b