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THE FATIGUE OF CARTILAGE IN THE PATHOGENESIS OF OSTEOARTHROSIS

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There seems no reason to think that osteo-arthrosis represents a single disease entity: indeed it should probably be viewed as a condition analogous to heart failure, a pathological process with an approximately unitary end point but numerous aetiologies. Only one of these possible aetiologies is discussed here, namely a sequence of events which it is suggested may result in cartilage damage and thereafter in destruction of the joint. It will be suggested that this sequence of events may be responsible for osteo-arthrosis in several joints, but in particular that it may be responsible for many examples of so-called idiopathic osteo-arthrosis of the hip.

General clinical experience creates the strong impression that many examples of secondary osteo-arthrosis are caused initially by some mechanical abnormality in the joint. Thus, for example, persistent talar tilt in the ankle following ligamentous injuries may cause osteo-arthrosis in the ankle; meniscectomy, which is known to increase the contact pressures on the meniscectomised side of the joint, also increases the chances of osteo-arthrosis developing in that side of the joint; incongruity at the hip either acquired during childhood or of congenital origin may similarly be presumed to increase the contact pressures by reducing the contact area in the hip, and such incongruous hips are known to be more liable to develop osteo-arthrosis than is a normal hip. In the upper limb, osteo-arthrosis in the elbow is rare but occurs as an occupational disease in pneumatic drill operators who sustain multiple blows to their elbows. It seems, therefore, reasonable to suppose that there might be a mechanical factor at work in the genesis of idiopathic osteo-arthrosis of the hip. Since idiopathic osteo-arthrosis is more common in the hip than in other joints, at least in

Caucasian man, this unknown mechanical factor might be thought to operate particularly in the hip as against other joints. Idiopathic osteo-arthrosis is also clearly age-related, being more frequent with advancing years. Thus it might be supposed that there is an age-related change affecting all joints and that this combines with some factor present in certain Caucasian hips to produce idiopathic osteo-arthrosis in that joint.

Mechanically, two tissue elements cooperate to produce the mechanical properties of articular cartilage: collagen and proteoglycan with its retained water. The collagen network confers tensile strength and stiffness upon articular cartilage and retains the proteoglycan gel by trapping it within the collagen meshwork. Finally, the collagen bonds the cartilage to the bone. Proteoglycan complexes appear to be trapped because they are of such a size that they are unable to move through the collagen network, but the possibility that they are bonded to collagen in some more direct way still remains open. The proteoglycans are strongly hydrophilic and therefore tend to draw water into the cartilage matrix. Direct measurements suggest that this pressure is of the order of 3½ atmospheres (Maroudas 1975). Cartilage does not, of course, expand when immersed, because the tendency to swell is resisted by the collagen network within which tensile stresses must be presumed to develop. Thus, unloaded cartilage consists of an hydraulically pressurized proteoglycan gel trapped within a collagen meshwork which is pre-stressed in tension. Thus, broadly speaking, the compressive properties of articular cartilage are proportional to the amount of proteoglycan in the matrix, whilst the tensile properties are proportional to the structure (as well as to the actual amount) of collagen.

It has been known for many years that the matrix of fibrillated cartilage is proteoglycan-depleted and it has therefore been thought that one possible cause of osteo-arthrosis might be proteoglycan depletion due to some cellular abnormality, followed by softening of the matrix and fibrillation. With methods of proteoglycan analysis which permit estimations to be made on small pieces of tissue (rather than on bulked areas of the matrix), it is now known that in fact proteoglycan depletion rarely if ever precedes fibrillation (Maroudas et al. 1973). If proteoglycan depletion does not precede fibrillation it seems unlikely that it causes it. The alternative possibility has to be considered, namely that some other factor acts upon articular cartilage to produce both fibrillation and proteoglycan depletion simultaneously.

The tensile properties of human adult articular cartilage have been extensively studied in my laboratory by Kempson and co-workers. Kempson (1973) has shown that the tensile properties vary from the surface through the deeper layers and that this variation can be correlated with the variation in the collagenous composition of cartilage. Kempson has also shown that in the surface the tensile properties are strongly directional, and once again this can be explained as being due to the orientation of collagen in the surface. The tensile properties appear to vary from joint to joint and from one site to another in the same joint. Thus before the effect of, for example, fibrillation or ageing can be related to the tensile properties of the cartilage, it is necessary to ensure that the variables mentioned above have been controlled in any comparison. When these variables are so controlled, a change can be demonstrated in the tensile strength and stiffness of articular cartilage with increasing age, at least in the knee (Kempson 1974). This change takes the form of diminishing strength and diminishing stiffness as age advances. Since osteo-arthrosis and the incidence of fibrillation both increase with increasing age, the question arises: can this loss of the normal tensile properties of articular cartilage be related to the genesis of osteoarthrosis?

Cartilage in life is not loaded statically to destruction as was (necessarily) the case in Kempson's experiments: on the contrary, it is loaded cyclically and in compression normal to the surface. Cyclical loading raises the possibility of fatigue failure, a phenomenon familiar in many areas of engineering. Fatigue is the process by which a loaded structure may fail mechanically in the face of a load of a given magnitude applied on numerous occasions, whereas a load of the same magnitude applied on one occasion does not produce failure. Since cartilage is loaded cyclically in life, it becomes important to establish whether or not cartilage is fatigue-prone. The possibility that the tissue is fatigue-prone is by no means far-fetched in view of the fact that bone is known to be fatigue-prone in the laboratory (Swanson et al. 1971), in clinical practice (Morris & Blickenstaff 1967), and on the basis of pathological observations (Todd et al. 1972). Since bone and cartilage are essentially composed of the same tissue elements, with the addition of hydroxyapatite in the case of bone, it becomes a possibility that cartilage, like bone, is fatigue-prone.

Weightman, also working in my laboratory, has studied the fatigue properties of human adult articular cartilage both in tension and in compression. In tension, Weightman has demonstrated: firstly, that cartilage is indeed fatigue-prone, and secondly, that the fall in fatigue resistance with age is so marked that tissue from cadavers of 20-year-olds would not be expected to fail after the application of 100 million cycles at a stress of 5 MN/m^2, whereas this stress would produce failure in the tissue of cadavers 50 years of age after application of the order of 10 million cycles (Weightman 1975). Although the tensile stresses occurring in articular cartilage in life are unknown, stresses of this order of magnitude seem likely to occur at least in certain hips.

Weightman has also studied the effects upon cartilage of a cyclically-applied compressive load (Weightman et al. 1973). This experiment does not give a sharply defined end point and therefore does not permit a quantitative result to be obtained. It was, however, demonstrated that a cyclically-applied compressive load produces fragmentation of the surface of the loaded cartilage, an appearance similar to fibrillation.

It is now suggested that fibrillation and hence osteoarthrosis may be due to fatigue failure in the collagen network of articular cartilage and that the reason why this condition becomes more frequent with increasing age is perhaps partly that the passage of time permits the application of a large number of loads to cartilage but that also, perhaps more importantly, the fatigue resistance diminishes sharply with age in a fashion which cannot be entirely explained as being due to the previous loading history of the tissue. There remains the question: what is the factor in some apparently normal hips which may be responsible for the genesis of fibrillation and hence of osteoarthrosis in Caucasian man?

In an attempt to answer this question, Day, Swanson and I have measured the contact pressures in various areas of the human cadaver hip (Day et al. 1975). We were able to show that the zenith of the young adult acetabulum frequently fails to make contact, not only at low loads as reported by Bullough et al. (1973), but also at loads of up to three times the body weight. In contrast, in more elderly hips the whole of the acetabulum makes contact at low loads and also at loads of three times the body weight. In a number of hips at all ages an anatomical feature was found in the zenith of the acetabulum which, when present and making contact, frequently resulted in the generation of very high contact pressures, i.e. pressures up to three times the average pressure in the hip as a whole. This feature consisted of an area, roughly triangular in shape, of thin fibro-cartilage at the zenith of the articular surface of the acetabulum. The origin of this feature is unknown but its presence has been commented upon by several workers.

In summary, the hypothesis is now advanced that fibrillation, and hence some cases of osteoarthrosis, may be due to fatigue failure in articular cartilage and that this phenomenon is age-related because the fatigue resistance of the collagen network in articular cartilage diminishes sharply with increasing age. The fall in the tensile stiffness and strength of articular cartilage is compatible with this view and suggests that, although the amount of collagen in the matrix of cartilage does not diminish with increasing age nor with the onset of osteoarthrosis, the mechanical integrity of the network is nevertheless failing. These findings would be compatible with the speculation that although the amount of collagen in the network was unchanged, the fibres or the cross-links between them were breaking. Once the surface has become fragmented and the network which normally retains the proteoglycan has been disrupted, proteoglycan depletion may occur by simple leakage as a secondary consequence. It is further suggested that the reason why this process develops with such frequency in certain Caucasian hips is that these hips contain an anatomical feature, namely a thin area of fibrocartilage at the zenith of the acetabulum, which is responsible for the generation of very high contact stresses in some joints.

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