Hypothesis Article

Conditioning of cartilage during normal activities is an important factor in the development of osteoarthritis

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Mechanical factors have long been implicated in the aetiology of osteoarthritis (OA). The two most popular hypotheses regarding the mechanism of cartilage damage are: the application of too high a stress and the mechanism of fatigue. Mechanical failure in any material, however, can be caused by either or both of these mechanisms. It is hypothesized that, because cartilage is a living tissue, the threshold at which it fails by either mechanism is regulated by the prevalent stresses arising in a joint. As these stresses are determined by activities and lifestyles, a low failure threshold can be the result of prolonged periods of low-level activity, which, if interrupted with short periods of intense activities, can subject weakened cartilage to damaging stresses. Were this hypothesis proven, it would address difficulties encountered with these hypotheses and explain some clinical observations. It would also have implications for the activities and lifestyles of individuals.

Factors often implicated in the development of osteoarthritis (OA) comprise those that increase the susceptibility to the disease (including age, sex, heredity, ethnic characteristics, hypermobility and osteoporosis) and those which have been directly implicated in causing mechanical damage to the articular cartilage. Amongst these latter factors are obesity (albeit controversial) [1], trauma, muscle weakness, joint deformation and repetitive use (whether occupational or leisure) [2, 3]. These are termed mechanical factors because they affect both the level and the manner in which joints are loaded and the cartilage stressed. Two major hypotheses underlie these factors: the hypothesis of too high stress and the hypothesis of fatigue. Both of these are discussed in this article, which is concerned with the mechanism by which the earliest damage to cartilage is caused by mechanical stresses arising in normal daily activities. The article is concerned neither with damage caused by abnormally high stresses arising in trauma nor with subsequent degeneration observed in the natural history of the disease.

Mechanical failure of cartilage: review of traditional hypotheses

Freund [4] proposed that there is a certain range of loading of cartilage that is conducive to its health; above and below this the tissues suffer. However, the view that cartilage will be damaged when subjected to too high stresses is as true of cartilage as it is of any biological tissue or engineering component, and so this view is not useful beyond saying that trauma is instrumental in damaging articular surfaces of a joint and bringing about the disease. Further, and more importantly, it does not define a safe upper limit for such stress for cartilage, which raises the question of whether this upper limit can be the same for two individuals of the same age, one active in sport and the other sedentary, or whether it can be the same for two individuals of similar occupations but of widely different age.

The opposite idea has also been suggested: that it is too little rather than too much stress that initiates the osteoarthritic process [5, 6]. The latter study cited the ‘odd’ medial facet of the patella where degenerative changes have been observed, but which are non-progressive and rarely advance beyond overt fibrillation [7]. This facet of the patella comes into contact with the femur at knee flexion angles above 135°, which is greatly beyond where the knee is flexed during ambulatory and most sedentary activities. The degenerative surface changes observed in this facet were thus attributed to habitual disuse, but no mechanism of how these changes occurred was described.

Fatigue was proposed as a mechanism of failure of articular cartilage [8]; this is likely to be a tensile failure of the collagen meshwork, either as a result of a single application of a large load (such as that which might occur in trauma) or of cumulative cyclic application of a lower load (such as that which occurs in normal daily activities). Later, in discussion of their hypothesis about the aetiology of OA, Freeman and Meachim [9] proposed that the increasing incidence of fibrillation with age may be accounted for by an increased rate of inception of fragmentation in the fibre network, due to diminishing fatigue strength in that network with age and the virtual absence of any capacity for repair. This view is in accordance with two studies [10, 11], both of which demonstrated that cartilage exhibits typical fatigue behaviour and showed further that fatigue resistance decreased with advancing age (Fig. 1a) (however, the correlation of fatigue fracture stress with age is somewhat tenuous; see legend of Fig. 1). Again, it is expected that cartilage, like all materials, is susceptible to fatigue failure. What is remarkable is the considerable scatter in the data; on examining the two fatigue studies, there are individuals between the ages of 20 and 60 yr with equally good and equally poor cartilage resistance to fatigue. More remarkable is the scatter in the age-related values of the tensile properties of intact cartilage in Kempson’s study on the knee [12] and later on the hip and ankle [13]. For instance, in the hip [13], the tensile fracture stress of the
A study [14] undertaken on the osteoarthritic lesions that are observed on the patello-femoral compartment of the knee joint during normal daily activities. Such scatter and, more importantly, overlap of ranges of values describing cartilage properties within widely separate decades of life may not be solely attributable to normal biological variations.

Below we discuss a hypothesis (which has been formulated and tested in a series of cadaveric studies) that implicates, in cartilage damage, an adaptive mechanism linking cartilage properties with the mechanical stimuli to which it is exposed during normal daily activities.

**Mechanical conditioning of articular cartilage**

A study [14] undertaken on the osteoarthritic lesions that are observed on the patello-femoral compartment of the knee joint (point 6) is considered an outlier and eliminated from the data but also a much slower decline in the tensile fracture stress with age. Such scatter and, more importantly, overlap of ranges of values describing cartilage properties within widely separate decades of life may not be solely attributable to normal biological variations.

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Ankle stresses (MPa) occurring in the various areas in the knee and ankle joints (from reference [17]).

<table>
<thead>
<tr>
<th>Specific joint surfaces</th>
<th>Overall mean creep modulus (MN/m²)</th>
<th>Predominant stress (MPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ankle</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Talar surfaces</td>
<td>11.20</td>
<td>2.0–5.0</td>
</tr>
<tr>
<td>Tibial surfaces</td>
<td>11.02</td>
<td>2.0–5.0</td>
</tr>
<tr>
<td>Knee</td>
<td>9.48</td>
<td>1.5–2.0</td>
</tr>
<tr>
<td>Femoral condyles</td>
<td>8.59</td>
<td>1.5–2.0 (mean, 1.57)</td>
</tr>
<tr>
<td>Tibial condyle covered by menisci</td>
<td>6.28</td>
<td>1.0</td>
</tr>
<tr>
<td>Patellar surfaces of femur</td>
<td>4.47</td>
<td>0.1–2.7 (mean, 0.97)</td>
</tr>
<tr>
<td>Tibial condyle not covered by menisci</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The first study [17], on two groups of knee and ankle joints, showed that the cartilage from the ankle tibio-talar joint was stiffest (had the highest compressive modulus) and that from patellar surfaces of the femur had the lowest stiffness. On ranking the various joint areas in descending order of cartilage stiffness (i.e. that with the highest compressive modulus first and that with the lowest last), the corresponding predominant stress acting on these areas followed the same ranking order (Table 1).

Because the cadaveric knees and ankles in that study were from different populations and because the stresses acting on the various areas tested were not measured directly but rather taken as those reported in other studies, the second study [18] was undertaken on a group of knees and ankles from the ipsilateral side. In this study, the stresses arising in these joints were determined experimentally. This second study confirmed the results of the first.

The cadaveric studies [14, 17–19] have thus confirmed that in the three major joints of the lower limb there is a correlation between the prevalent stresses arising during locomotion in the different joint areas and the cartilage properties in these areas. These studies, however, do not prove the proposed hypothesis, but rather provide the necessary (but not sufficient) circumstantial evidence that it might be true.

A rigorous test of the hypothesis should aim to induce, in living joints, cartilage fibrillation similar to that observed in early OA. This test would be undertaken on an animal model in which the animals would be put through controlled exercise regimens that produced in the joints the stress patterns implicated in the aetiology of OA, as the present hypothesis proposes. Four groups would be necessary. The first of these would be a control animal that is allowed to roam freely. The second would be subject to constraints reducing the level of activity and in turn the mechanical stress acting on the joints. The third would be encouraged to increase its degree of activity to increase the level of stress. By measuring the mechanical properties of cartilage in these three groups it would be possible to ascertain whether the reduction in the level of activity of the second group (below that of the first control group) had resulted in a corresponding reduction in cartilage stiffness, and that an increase in the level of activity in the third had resulted in a corresponding increase in cartilage stiffness. The fourth group would then be subjected to a regimen of alternately prolonged periods of reduced joint stress (causing deterioration in cartilage properties) and occasional short periods of strenuous exercise, inducing high stresses on the joints. It would then be possible to ascertain whether this regimen would induce fibrillated lesions in articular cartilage.

Despite this difficulty, the following important clinical observations that are not adequately explained by the stress and fatigue hypotheses can be explained by the proposed hypothesis (were it proven true).

(i) In the cadaveric studies from the author’s group, osteoarthritic lesions were observed in some of the knee joints—on the patellar surfaces of the femur and on the areas not covered by the menisci. These two areas are predominantly subject to low stresses, but occasionally to much higher stresses. No OA lesions were observed in the tibio-talar joints of the ankles tested. It is especially noteworthy that the tibio-talar joint in the ankle, which has the lowest incidence of OA [21–25], is also predominantly subjected to high stresses [26]. The reasons for this predominance of high stresses in the tibio-talar joint are: (a) loads of similar magnitudes to those acting on the knee act on the tibio-talar joint but are distributed on much smaller articular surfaces than those of the knee; and (b) the tibio-talar joint has a much smaller range of movement and a relatively simple and congruous geometry, which cause almost its entire surface to be stressed during locomotion.

(ii) The increased incidence of OA in knees after meniscectomy [27, 28] can be explained as a result of the large and sudden increase in the stresses acting on the areas not covered by the menisci due to the transfer of the entire load that acts in the tibiofemoral joint onto these areas after the removal of the menisci [29, 30].

(iii) The reported increase in incidence of OA lesions in the inferior third of the patellar surface [31] (which is loaded at the lower angles of knee flexion) in anterior-cruciate-deficient knees can be explained by increased stresses in this area as a result of altered tracking of the patella.

(iv) The mild damage observed in the ‘odd’ facet of the patella that is not habitually stressed [6] can be the result of the infrequent application of high stress when this area comes into contact with the femur during such activities as squatting and rising up from a deep squat, which are relatively rarely practised in the West and during which large loads arise in the joint [32].

(v) The scatter of the cartilage properties and, in particular, the fatigue resistance observed within the various decades of life [10–13] can be explained by mechanical conditioning of cartilage as a result of the different lifestyles: more active older individuals would have stiffer/stronger and healthier cartilage with higher failure thresholds than younger sedentary individuals.

**Implications of the hypothesis**

In conclusion, the conditioning hypothesis proposes that degenerative changes in cartilage that can lead to OA might be associated with a Western lifestyle, in which many people exercise in short sharp bursts, often undertaking different sports, each of which is interspersed with long periods of inactivity. This hypothesis thus holds that individuals might be responsible to a large extent for the state of health of their cartilage, and implies that regular exercise might better maintain cartilage in good health. It also implicitly advises against sudden increases in the
level of activity, but recommends instead a gradual increase when changing from a sedentary lifestyle to an athletic one. The need for epidemiological studies into the association between OA and activity is underscored.

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References