Chapter 3
Pathophysiology of osteoarthritis

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Anatomy of normal joints

Human movement is made possible by synovial fluid, or freely moving, and cartilaginous, or fixed, joints [1]. The synovial joint is a functional connective tissue unit that allows two opposed limb bones to move freely in relation to each other. The bone−cartilage−synovial fluid−cartilage−bone assembly can be regarded as a continuum, with the load-bearing structures organised differentially depending on site and function, resulting in a specialised joint structure [1].

There are five basic types of structures in the knee (Figures 3.1 and 3.2, see page 36) [2–5]:

• ligaments, which are passive elastic structures that can be loaded in tension only;
• musculotendinous units, which are active elastic structures that act only under tension;
• cartilage and subchondral bone, which accommodate the compressive loads of the joint;
• menisci, which are crescentic fibrocartilaginous pads that attach to the intercondylar area and periphery of the tibial plateau; and
• the bursae.

Figure 3.1 Anterior and lateral view of the normal knee anatomy.
A, image showing the basic structure of the knee. Ligaments can be divided into intra-articular and extracapsular.
B, The major bursae around the knee. Adapted with permission from Niitsu [5].

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Pathophysiology

Osteoarthritis is considered an organ disease that involves the whole joint structure. A gradual loss of articular cartilage in synovial joints is combined with subchondral bone sclerosis, osteophytes at the joint margins and mild, chronic nonspecific synovial inflammation [6,7]. A hypothetical model of the development of osteoarthritis is shown in Figure 3.3 [6].

Hypothetical model for initiation and perpetuation of osteoarthritis

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Ageing cartilage</th>
<th>Initiation</th>
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<tbody>
<tr>
<td>Excessive weight</td>
<td>Cartilage fissure</td>
<td>Deleterious mechanical stresses</td>
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<tr>
<td>Injury and occupation</td>
<td>Shorter glycosaminoglycan</td>
<td>Genetic factors</td>
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<tr>
<td>Developmental deformities</td>
<td>Increased KS6 concentration/decreased KS4 concentration</td>
<td>Hormonal factors?</td>
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<tr>
<td>Joint laxity</td>
<td>Decrease in chondrocyte number</td>
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<td></td>
<td>Accumulation of advanced glycation end products</td>
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<td></td>
<td>Decrease in water concentration</td>
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<tr>
<td></td>
<td><strong>REVERSIBLE</strong></td>
<td></td>
</tr>
<tr>
<td>Early osteoarthritis</td>
<td><strong>IRREVERSIBLE</strong></td>
<td></td>
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<tr>
<td>Increased chondrocyte proliferation</td>
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<td></td>
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<tr>
<td>Increased synthesis of matrix by chondrocytes</td>
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<td></td>
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<tr>
<td>Alteration in collagen synthesis (decrease in type II/type I collagen ration)</td>
<td></td>
<td></td>
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<tr>
<td>Chondrocyte dedifferentiation</td>
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<tr>
<td>Increased synthesis of proteinases by chondrocytes</td>
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<td>Increased synthesis of cytokines by chondrocytes</td>
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<tr>
<td>Subchondral bone demineralisation with microfractures</td>
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<tr>
<td>Inflamed synovial tissue</td>
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<tr>
<td>Late osteoarthritis</td>
<td>Decreased chondrocyte proliferation</td>
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<tr>
<td>Chondrocytes apoptosis</td>
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<tr>
<td>Hypertrophic differentiation of chondrocytes</td>
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<td>Osteophyte formation</td>
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<tr>
<td>Bone sclerosis</td>
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<td>Persistence of proteinases and cytokines synthesis</td>
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</tbody>
</table>

Figure 3.2 Plain radiograph of the normal right knee. This radiograph clearly shows the femur, tibia and fibula. The patella can be seen as faint circular outline overlapping the femur, centred at the widest part of the femur. Image from Abdul-Jabar et al [4].

Figure 3.3 Hypothetical model for initiation and perpetuation of osteoarthritis. Accumulation of risk factors on ageing cartilage triggers the initiation of the osteoarthritis process. For didactic reasons, two phases are described, early osteoarthritis and late osteoarthritis, but the passage from one to the other is progressive and generally lasts many years. KS, keratan sulphate. Reproduced with permission from Berenbaum [6].