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Joint Injury, Repair, and Remodeling

Roles in Post-Traumatic Osteoarthritis

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Joint injuries, especially intraarticular fractures, frequently lead to progressive joint degeneration that causes the clinical syndrome of posttraumatic osteoarthritis. Orthopaedists try to prevent this disease by attempting to restore joint congruity, alignment, and stability; however, many patients have crippling joint pain and dysfunction develop despite optimal current treatment. The pathophysiology of posttraumatic osteoarthritis has not been explained. It is not simply the magnitude and type of injury that determines whether an injured articular surface will repair and remodel or undergo progressive degeneration. For these reasons, clinically significant progress in preventing posttraumatic osteoarthritis depends on advances in understanding of the pathogenesis of this disease that will make it possible to decrease the risk of articular surface degeneration and facilitate articular surface repair and remodeling. We examine the relationships between joint injury, repair and remodeling, and joint degeneration; the factors that increase the risk of posttraumatic joint degeneration; and, the questions that need additional investigation to develop treatments of joint injuries that will decrease the risk or severity of posttraumatic osteoarthritis.

Posttraumatic osteoarthritis (OA), the syndrome of joint degeneration, dysfunction and pain, that develops after joint injuries, is a common well recognized disorder.[47,48,74] Unlike idiopathic OA which primarily affects people older than 60 years, posttraumatic OA causes pain and disability for young and middle-aged adults and the elderly.[21,23,25,32,47] Older patients with crippling OA often can be treated effectively with joint replacement or joint fusion, and restriction of activity.[17,37,88] These approaches are not as acceptable or effective for young and middle--aged adults. For this reason, younger patients with posttraumatic OA present an especially difficult clinical problem.

Clinical experience and epidemiologic studies show that joint injuries including direct and indirect joint impact loading, meniscal, ligament and joint capsule tears, joint dislocations and intraarticular fractures, increase the risk of progressive joint degeneration that causes posttraumatic OA.[14,20,25,42,47,48,104] Basic scientific investigations have shown how mechanical forces damage articular surfaces and clarified the responses of articular surfaces to injury.[13,16,23,25] Other work has helped define the abnormalities in distribution and magnitude of joint contact stresses caused by residual articular surface incongruity and the capacity for remodeling of posttraumatic articular surface incongruity.[69,74]

Despite numerous experiments showing that joint injuries cause joint degeneration and extensive clinical experience with joint injuries and posttraumatic OA, understanding of this disease is limited. The relationship between articular surface injury severity and risk of joint degeneration have not been defined, and the mechanisms responsible for progressive loss of grossly normal articular surfaces after joint injuries have received little attention. Insufficient effort has been directed toward understanding the long-term results of the repair and remodeling responses of synovial joints after injury and how these responses could be promoted to decrease the risk of joint degeneration. Although joint instability seems to increase the risk of joint degeneration, there has been little experimental study of the role of posttraumatic joint instability in the development of articular surface degeneration. Furthermore, the risk of posttraumatic OA varies among joints and among individuals,[47] and investigators have been studying the reasons for the decreased capacity for healing of articular surface injuries with increasing age.[54,78–80,82,107,113] For these reasons, other than attempts to restore joint congruity, alignment, and stability, there are no treatments that decrease the risk or rate of progression of posttraumatic OA, and the efficacy of current treat-

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ments of many types of joint injuries has not been documented.[74]

The biologic events responsible for posttraumatic joint degeneration remain unknown and even books devoted to OA provide little or no information concerning posttraumatic OA,[10,88] possibly because many physicians and investigators assume that joint degeneration after injuries is the consequence of irreversible mechanical damage. Yet, this assumption has not been proven; and, if it is true, the types of injuries that lead inexorably to joint degeneration have not been defined. Advances in the prevention and treatment of posttraumatic OA depend on increased understanding of the pathophysiology of this disorder. We first examined the relationships between joint injury, repair and remodeling, and the development of joint degeneration. We then reviewed current understanding of the factors that increase the risk of posttraumatic OA by compromising articular surface repair and remodeling and the issues that need additional investigation to develop treatments that will decrease the risk or severity of posttraumatic OA.

Acute Mechanical Injuries of Articular Surfaces

Synovial joints are formed from articular cartilage, subchondral and metaphyseal bone, synovium, ligaments, and joint capsules.[22,24] The articular surfaces, consisting of articular cartilage supported by subchondral bone and metaphyseal trabeculae, not only serve as superb low-friction gliding surfaces, they effectively distribute loads across synovial joints.[22,25] The mechanical properties of articular cartilage depend on the two principal components of the articular cartilage matrix, the solid macromolecular framework, consisting primarily of collagens and aggregating proteoglycans (PGs), and the water within this macromolecular framework. The collagens give the tissue its form and tensile strength, and the interaction of aggregating PGs with water give the tissue its stiffness to compression, resilience, and durability.[22] Articular cartilage tolerates loading resulting from normal daily activities so well that in many individuals it shows little or no evidence of degeneration after 8 decades or more of daily use.

Disrupting a normal articular surface with one impact requires substantial force, presumably because of the ability of articular cartilage and the supporting bone to dampen and distribute loads. A transarticular load of 2170 N applied to patellofemoral joints in canines caused fractures in the zone of calcified cartilage visible by light microscopy and articular cartilage fissures that extended from the articular surface to the transitional or superficial radial zone of the articular cartilage.[109] A study of the response of human articular cartilage to blunt trauma showed that articular cartilage could withstand impact loads of as much as 25 N per square millimeter (25 MPa) without apparent damage. Impact loads exceeding this level caused chondrocyte death and cartilage fissures.[103] The authors suggested that reaching a stress level that could cause cartilage damage required a force greater than that necessary to fracture the subchondral bone. Another study[51] measured the pressure on patellofemoral articular cartilage in humans during impact loading and showed that impact loads less than the level necessary to fracture bone caused stresses greater than 25 MPa in some regions of the articular surface. With the knee flexed 90°, 50% of the load necessary to cause a bone fracture produced joint pressures greater than 25 MPa for approximately 20% of the patellofemoral joint. At 70% of the bone fracture load, approximately 35% of the contact area of the patellofemoral joint pressures exceeded 25 MPa, and at 100% of the bone fracture load, 60% of the patellofemoral joint pressures exceeded 25 MPa. One study of the effects of impaction damage to articular cartilage showed that stresses of 15 MPa to 20 MPa caused chondrocyte death and rupture of the articular cartilage collagen fibril network.[110]

Although the magnitude of the applied force is important in determining the extent of articular surface damage,[52,91] the orientation of the load relative to the articular surface[45] and the rate of loading[2,43,44,95,101] also are important. Slowly applied loads and suddenly applied loads differ considerably in their effects. The solid component of the matrix, primarily the collagen-PG macromolecular framework, and the fluid component, have roles in bearing loads applied to articular surfaces. After any but the most rapidly applied forces, loading of articular surfaces indents the cartilage and causes movement of matrix fluid and deformation of the macromolecular framework, events which dampen and distribute loads within the cartilage and decrease loading of the subchondral bone.[89] These changes decrease the stress applied to the cartilage macromolecular framework. When loading occurs too rapidly for fluid movement through the matrix, as with sudden impact or torsional loading of the joint, the matrix macromolecular framework sustains a greater force, and it is likely the chondrocytes are subjected to damaging levels of mechanical stress. If this force is great enough, it ruptures the matrix macromolecular framework,[59] damages or kills the cells,[63,110] and exceeds the ability of articular cartilage to prevent subchondral bone damage by dampening and distributing loads. For these reasons, the high rates of loading that occur during acute joint trauma may cause more tissue damage than more slowly applied loads of similar magnitude.

Types of Articular Surface Mechanical Injury and Responses to Injury

Based on the type of tissue damage, articular surface injuries caused by mechanical forces can be classified into three types (Table 1): (1) damage to the cells and matrices

TABLE 1. Chondral and Osteochondral Injuries

Injury	Evaluation	Repair Response	Potential for Healing
Damage to chondral matrix and/or cells without visible disruption of the articular surface	Inspection of the articular surface and current clinical imaging methods for articular cartilage cannot detect this type of injury MRI of subchondral bone may show edema	Synthesis of new matrix macromolecules Cell proliferation?	If the basic matrix structure remains intact and enough viable cells remain, the cells can restore the normal tissue composition If the matrix and/or cell population sustains significant damage or if the tissue sustains further damage, the lesion may progress to cartilage degeneration
Cartilage disruption (chondral fractures or ruptures)	CT and MRI imaging can show these injuries	No fibrin clot formation or inflammation Synthesis of new matrix macromolecules and cell proliferation, but new tissue does not fill the cartilage defect	Depending on the location and size of the lesion and the structural integrity, stability and alignment of the joint, the lesion may or may not progress to cartilage degeneration
Cartilage and bone disruption (osteochondral fractures)	CT imaging can show these injuries	Formation of a fibrin clot, inflammation, invasion of new cells and production of new chondral and osseous tissue	Depending on the location and size of the lesion and the structural integrity, stability and alignment of the joint, the repair tissue may remodel and serve as a functional joint surface or it may degenerate

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of articular cartilage and subchondral bone that is not associated with visible disruption of the joint surface; (2) visible mechanical disruption of articular cartilage limited to articular cartilage that takes the form of chondral fissures, flap tears or chondral defects; and (3) visible mechanical disruption of articular cartilage and bone, that is, intraarticular fractures.[3,7,13,16,23,28,29,46,111] Each type of tissue damage stimulates a different repair response.[13,29]

Cell and Matrix Damage

Articular cartilage damage that leaves the overlying articular surface intact occurs with almost every joint injury.[13,39,70,109,114] The intensity and type of joint loading that can cause chondral and subchondral damage without visible articular surface disruption has not been well defined. Physiologic levels of joint loading do not cause this type of joint injury, but impact loading above that generated by normal activities such as walking or lifting light objects, but less than that necessary to produce visible cartilage disruption, can disrupt cartilage matrix macromolecular framework, damage or kill chondrocytes, decrease PG concentration and synthesis, and increase the matrix water concentration and permeability.[18,11,13,35,39,41,43,56,57,70,109]

Experimental evidence suggests that increased degradation or decreased synthesis of aggregating PGs is the least severe cartilage injury caused by impact loading.[8,39,99] However, even this ostensibly minimal injury increases the risk of joint degeneration. Loss of PGs decreases cartilage stiffness and increases its permeability. These alterations may cause greater loading of the remaining macromolecular framework making the tissue more vulnerable to additional damage from loading including distortions or disruptions of the collagen fibril network and the collagen-PG relationships, swelling of the matrix,[39] and chondrocyte injury or death. Impact loading also may cause chondrocyte death directly.[13,38,63,70,100] Chondrocytes that survive a joint injury may have decreased ability to maintain and repair the tissue as a result of increased mechanical or metabolic stress.

The ability of chondrocytes to sense changes in matrix composition and synthesize new molecules makes it possible for them to repair damage to the macromolecular framework.[22,23,77,83] It is not clear at what point this type of injury becomes irreversible and leads to progressive loss of articular cartilage. Presumably, the chondrocytes can restore the matrix as long as the loss of matrix PG does not exceed what the cells can rapidly produce, if the fibrillar collagen meshwork remains intact and if enough chondrocytes remain capable of responding to the matrix damage. When these conditions are not met the cells cannot restore the matrix, the chondrocytes will be exposed to

excessive mechanical and metabolic stresses and the tissue will degenerate.

Cartilage Disruption

Chondrocytes respond to injuries that disrupt articular cartilage, but that do not extend into subchondral bone (Table 1). After this type of injury they proliferate and increase synthesis of matrix macromolecules near the injury; but, the newly synthesized matrix and proliferating cells do not fill the tissue defect, and soon after injury the increased proliferative and synthetic activity ceases.[23,27,28] This leaves a permanent articular surface defect that can alter joint mechanical function and increase the risk of joint degeneration.

Cartilage and Subchondral Bone Disruption (Intraarticular Fractures)

Unlike injuries limited to cartilage, injuries that extend into subchondral bone cause hemorrhage and fibrin clot formation, and activate the inflammatory response.[27,28,86] As a result, the repair and remodeling of intraarticular fractures differs from the events that follow injuries that cause only cell and matrix injury or disruption of the articular surface limited to articular cartilage (Table 1). However, the force required to cause an intraarticular fracture causes cell and matrix damage and chondral disruption. For these reasons, intraarticular fractures include all three types of articular surface injury (Table 1).

The degree of displacement of the fracture and the size of the gaps between fracture fragments influence the extent and outcome of the repair and remodeling responses. In a study of experimental intraarticular fractures in adult rabbits, the investigators fractured the distal femoral articular surfaces.[86] They then reduced the fractures in three different fashions: incomplete reduction, anatomic reduction without compression of the fragments, and anatomic reduction with compression of the fragments. Chondral fractures that were reduced inadequately or that were reduced anatomically without compression healed by fibrocartilage. Chondral fractures that were reduced with compression of the fragments healed with tissue which, by light and electron microscopy, seemed to be hyaline cartilage. The authors suggested that compression of the cartilage surfaces creates a physical environment that allows chondrocytes to heal the defect, or, prevents ingrowth of granulation tissue from the subchondral bone and thereby allows healing with hyaline cartilage instead of fibrocartilage.

The repair of the chondral portions of intraarticular fractures with gaps between the fracture fragments has not been studied extensively, therefore the current understanding of this process is based on studies of osteochondral repair of experimental drill hole defects.[18,26] These studies show that soon after injury, blood escaping from the damaged bone blood vessels forms a hematoma that temporarily fills the injury site. Fibrin forms within the hematoma and platelets bind to fibrillar collagen. A continuous fibrin clot fills the bone defect and extends for a variable distance into the cartilage defect. Platelets within the clot release vasoactive mediators and growth factors or cytokines (small proteins that influence multiple cell functions including migration, proliferation, differentiation and matrix synthesis), including transforming growth factor-beta (TGF-β) and platelet-derived growth factor (PDGF). Bone matrix also contains growth factors such as TGF-β, bone morphogenic proteins (BMPs), (PDGF), insulin-like growth factor I (IGF-I), insulin-like growth factor-II (IGF-II), and possibly others. Release of these growth factors may have an important role in the repair of osteochondral defects. In particular, they probably stimulate vascular invasion and migration of undifferentiated cells into the clot, and influence the proliferative and synthetic activities of the cells.

Shortly after entering the tissue defect, the undifferentiated mesenchymal cells proliferate and synthesize a new matrix. Within 2 weeks of injury, some mesenchymal cells assume the rounded form of chondrocytes and begin to synthesize a matrix that contains Type II collagen and a relatively high concentration of PGs. These cells produce regions of hyaline-like cartilage in the chondral and bony portions of the defect. Six to 8 weeks after injury, the repair tissue within the chondral region of osteochondral defects contains many chondrocyte-like cells in a matrix consisting of Type II collagen, PGs, some Type I collagen and noncollagenous proteins. Unlike the cells in the chondral portion of the defect, the cells in the bony portion of the defect produce immature bone, fibrous tissue, and hyaline-like cartilage.[26] The bony repair tissue is well vascularized, but blood vessels rarely enter the chondral portion of an osteochondral defect. Six to 8 weeks after injury the chondral repair tissue typically has a composition and structure intermediate between hyaline cartilage and fibrocartilage; it rarely, if ever, replicates the elaborate structure of normal articular cartilage.[18,19,22,23,29]

Repair tissue that fills osteochondral defects is less stiff and more permeable than normal articular cartilage, and the orientation and organization of the collagen fibrils in even the most hyaline-like chondral repair tissue do not follow the pattern seen in normal articular cartilage.[26] In addition, the repair tissue cells may fail to establish the normal relationships between themselves and the matrix, and among matrix macromolecules; in particular, the organization of the pericellular, territorial, and interterritorial matrices, the concentrations of matrix macromolecules and the relationships between cartilage PGs and the col-

lagen fibril network appear abnormal in most samples of chondral repair tissue.[26] The decreased stiffness and increased permeability of repair cartilage matrix may increase loading of the macromolecular framework during joint use, resulting in progressive structural damage to the matrix collagen and PGs, thereby exposing the repair chondrocytes to excessive loads that additionally compromise their ability to restore the matrix.[26]

The capacity for remodeling of chondral repair tissue that forms after intraarticular fractures, and the mechanical and biologic factors that influence chondral repair tissue remodeling have not been studied rigorously. Experimental studies of osteochondral healing and clinical experience with patients with comminuted displaced intraarticular fractures and regain excellent joint function suggest that chondral repair tissue occasionally progressively remodels to form a functional joint surface.[15,16,18,23] However, in most large osteochondral injuries, the chondral repair tissue does not follow this course. Instead, it begins to show evidence of degeneration including depletion of matrix PGs, fragmentation and fibrillation, increasing collagen content, and loss of cells with the appearance of chondrocytes within 1 year or less.[16,18,23,29] The remaining cells often assume the appearance of fibroblasts as the surrounding matrix comes to consist primarily of densely packed collagen fibrils. This fibrous tissue usually fragments and often disintegrates, leaving areas of exposed bone. The inferior mechanical properties of chondral repair tissue may be responsible for its frequent deterioration.[15,23,26,27]

Remodeling of chondral repair tissue may vary with age. Chondrocytes in skeletally immature animals show a better proliferative response to injury and synthesize larger PG molecules than those from mature animals.[30,33,75–77,82] Furthermore, a growing synovial joint has the potential to reshape the articular surface to decrease the mechanical abnormalities created by a chondral or osteochondral defect.

Remodeling of Articular Surface Step-offs and Gaps

Intraarticular fractures create articular surface gaps or voids (regions where parts of the surface are missing or displaced) and step-offs (regions where the fractured articular surfaces are not at the same level). Large gaps or step-offs cause clinically apparent joint instability or malalignment or both, and have little or no potential for repair and remodeling that leads to a functional joint surface. In most instances large defects or step-offs can be reduced by manipulative or operative treatment to the extent that they do not cause obvious instability or malalignment.

Animal experimental work shows that articular step-offs and gaps that are not large enough to cause clinically apparent joint instability or malalignment have considerable potential for remodeling after repair of an osteochondral injury. Work by Llinas et al[69] and Lovasz et al[71] showed that 1-mm step-offs in the rabbit medial femoral condyle remodeled during a period of 12 weeks, and the elevated contact pressure caused by the step-off, decreased markedly with remodeling. The source of the cells responsible for the remodeling of the articular surface is not certain, but 12 weeks after injury they have the appearance of chondrocytes. A 1-mm step-off in this experiment represented the full thickness of the articular cartilage. The authors concluded that step-offs as great as the full thickness of the articular cartilage have considerable potential for remodeling that restores a nearly normal articular surface, but expressed concern that step-offs greater than the thickness of the articular cartilage might not remodel as successfully.[69,71] A study by Lefkoe et al[68] showed that 3-mm wide fragments of rabbit femoral condylar articular surface depressed 2 mm remodeled over 20 weeks and resulted in restoration of a congruent cartilaginous articular surface. The authors concluded that their results call into question the value of anatomic reduction of intraarticular fractures in decreasing the risk of posttraumatic OA.

Although these studies document that there is substantial potential for remodeling of intraarticular step-offs and gaps in stable joints with isolated injuries, it is unclear how articular surface remodeling is influenced by the severity of the initial injury, age, joint shape and congruency, cartilage thickness, and cartilage biologic and mechanical properties. Nor is it clear how rigid internal fixation of intraarticular step-offs and gaps affects remodeling of the articular surface.

Risk Factors for Posttraumatic Joint Degeneration

The explanation for why some injured joints return to near normal structure and function whereas others degenerate lies to some extent in understanding the factors that interfere with joint surface repair and remodeling, and cause grossly normal articular cartilage to degenerate after a joint injury. Better understanding of these factors could improve current efforts to treat joint injuries and prevent posttraumatic joint degeneration and lead to new approaches to decrease the risk and severity of joint degeneration after injury.

Severity of Injury

Based on in vitro and in vivo experimental studies of the effects of impact loading of articular surfaces, it is reasonable to assume that more intense acute impact loading of articular surfaces causes more extensive chondrocyte death and matrix damage.[13,16,63] Presumably, more extensive chondrocyte death increases the risk of joint degen-

eration. However, these assumptions have not been tested in rigorous experimental studies, nor has it been shown that the intensity of loading of articular surfaces is correlated with the risk of posttraumatic OA. Observational studies of the outcomes of intraarticular fractures suggest that more extensive comminution of articular surfaces and greater initial displacement of the fracture fragments increase the risk of joint degeneration.[47,74] These studies do not show whether it is the severity of the initial injury, that is, the energy transferred to the joint surfaces, greater residual irregularity of the articular surface, less effective joint surface repair and remodeling, or combinations of these factors, that increase the risk of joint degeneration.

Residual Articular Surface Incongruity

In addition to the acute articular surface damage caused by impact, torsional or shear loading, intraarticular fractures may leave residual articular surface irregularities that cause chronic increased contact stress. Brown et al[12] examined the effects of experimentally created step-offs of tibial articular surfaces in humans on peak pressure levels using pressure-sensitive Fuji film. They showed that peak local pressure near the ledge on the high side of the step-off generally increased with increased step-off, but that statistically significant pressure increases did not occur until the step-off exceeded 1.5 mm. Even 3-mm step-offs only led to local peak pressure 75% greater than normal, and Brown and colleagues estimated that the tibial articular surface could tolerate long-term local pressure that was twice the normal value. One of the other important findings reported by Brown and colleagues was that tibial articular surface specimens varied considerably in their sensitivity to step-offs.[12] In some specimens, minor step-offs, that is, 0.25 mm, produced high local peak pressures whereas in other specimens 3-mm step-offs had little effect. The authors showed that the sensitivity to step-offs correlated inversely with cartilage thickness ($r = -0.58$). These observations suggest that joints with the same step-off after an intraarticular fracture vary greatly in the risk of chronic deleterious levels of contact stress. Bai et al[4] studied the effects of lateral tibial plateau articular surface step-offs from 1–6 mm and meniscectomy on knee alignment and contact pressures. They showed that progressively greater articular step-off heights increased valgus angle and contact pressure. They also showed that meniscectomy additionally increased the valgus angle and contact pressures.

The results of clinical studies of the risk of posttraumatic OA after tibial plateau fractures are consistent with these experimental studies. They suggest that increasing step-offs increase the risk of posttraumatic degenerative disease of the knee, but they do not clearly show that step-offs above a critical level consistently lead to OA or that reduction of step-offs below a critical level reduces the risk of OA.[6,9,53,54,67,102] They also suggest that for most patients, meniscectomy is an important factor in increasing the risk of joint degeneration after tibial articular surface injuries of the knee.[54] Other similar studies of acetabular surface incongruity show that increasing step-offs and gaps in the acetabular articular surface increase contact stress and instability.[50,66,96–98,108,112] These studies do not clarify the role of the severity of the initial injury compared with the role residual joint surface incongruity in determining the risk of posttraumatic OA. Methods of calculating the energy transferred to the articular surface and the stresses caused by irregularity of the articular surface in humans with intraarticular fractures would make it possible to determine the relationships of these factors to the risk of joint degeneration.

Residual Joint Instability

Joint instability refers to abnormal motion of a joint caused by failure to maintain the joint surfaces in normal apposition throughout the range of motion (ROM), or subluxation or dislocation of joint surfaces after application of less force than would be required to separate the articular surfaces of a normal joint. Causes of posttraumatic joint instability include ruptures of ligaments, menisci and joint capsules, or articular surface gaps and step-offs. The abnormal movements that occur in unstable joints have not been well defined and they are difficult to measure precisely. Based on clinical examination they are described as translational (when joint surfaces slide past each other, for example, the anterior movement of the tibial articular surface of the knee relative to the femoral surface in a knee that lacks an ACL) and rotational (when joint surfaces rotate past each other, for example, the pivot shift movement in knees that lack an ACL).[1,34,40,60,64,65]

Experimental models of joint degeneration show that mechanical instability of the knee created by ACL transection and menisectomy can lead to progressive joint degeneration in otherwise normal joints.[36,84,85,87] Other experimental work suggests that the combination of instability and articular surface incongruity are more likely to cause progressive joint degeneration than either condition alone. In rabbits, transection of the ACL caused rapid progressive loss of articular cartilage on the high side of a 0.5-mm intraarticular step-off: animals with an intact ACL did not have degenerative changes.[72] Joint instability combined with impaired joint sensory innervation may increase the susceptibility of joints to degeneration.[92–94] Experimental studies showed that partial loss of joint innervation accelerated the development of degenerative joint disease in dogs with ACL transection. These observations suggest that partial joint denervation caused by tearing of the periarticular soft tissues or extensive surgical dissec-

tion could accelerate the development of posttraumatic joint degeneration.

Clinical studies also indicate that joint instability caused by ligamentous injury increases the risk of joint degeneration.[5,49,58,61,62,73,105,106] In one clinical study, age at the time of knee ACL and MCL injury influenced the risk of joint degeneration: at 9–16 years after ACL rupture, 58% of patients who were younger than 35 years at the time of injury had evidence of joint degeneration compared with 87% of the patients who were older than 35 years at the time of injury.[106]

The available experimental and clinical studies have not defined the mechanisms responsible for degeneration of the articular surface in unstable joints, but possible adverse effects of joint instability include increasing the number and intensity of rapid impact loadings and increasing shear and compression forces on regions of the joint surface. Use of some unstable joints causes the articular surfaces to separate and then come together with considerable force, or lurch past each other, events that patients often describe as "giving way." Episodes of abnormal articular surface separation or giving way in unstable joints usually occur rapidly and unexpectedly. These sudden jerking or lurching joint movements may cause high levels of localized articular surface contact stress that would interfere with articular surface repair and remodeling and cause degeneration of grossly normal articular cartilage.[13,16,23,90]

Differences Among Joints

The probability of progressive joint degeneration after injury may vary among joints.[47] For example, preliminary studies suggest that the ankle is at increased risk of posttraumatic OA relative to the knee, but is at less risk of primary OA.[31] A study by Huber-Betzer et al[55] helps explain why joints could vary in the risk of posttraumatic OA caused by residual incongruity, malalignment, or instability. The authors examined the effects of morphologic features of joints on contact stress elevation caused by imprecisely reduced intraarticular fractures by using a finite element model to evaluate changes in articular surface stress distributions caused by step-offs. Decreased cartilage thickness and increased cartilage modulus increased peak local contact stress. Decreased global joint congruity; for example, from decreased concavity of the tibial plateau, also increased local contact stress. This study strongly suggests that the sensitivity of a joint to incongruity may vary considerably among joints depending on the thickness and modulus of the articular cartilage and joint global congruity. In addition to differences in sensitivity to incongruity and instability, joints may vary considerably in their ability to repair and remodel their articular surface. Taken together these differences may help explain variability among joints in the outcomes of intraarticular fractures[47,74] and suggest that optimal treatment of injuries will vary among joints.

Patient Age

Age seems to be a risk factor for the development of posttraumatic OA.[16] Articular cartilage chondrocytes show a profound age-related decline in their ability to respond to anabolic stimuli, a change that may be caused by progressive cell senescence.[77–79,82] This observation suggests that the risk of posttraumatic OA increases with age as result of decreased ability of chondrocytes to maintain and restore articular cartilage.[81] Clinical studies support the hypothesis that age is an important risk factor for the development of posttraumatic OA. They show that patients older than 50 years have a twofold to fourfold greater risk of OA after intraarticular fractures of the knee[54,107,113] than younger patients, and that age increases the risk of knee degeneration after ACL.[106]

Limitations of Current Evaluation and Treatment of Articular Surface Injuries

Joint trauma that causes intraarticular fractures necessarily causes cell and matrix damage that is not visible and ruptures or tears articular cartilage (Table 1). All three types of articular surface injury may contribute to progressive joint degeneration after injury, but, because of current limitations in the diagnosis and treatment of joint injuries, orthopaedists treat only the intraarticular fractures. Improved imaging techniques have made it possible to accurately define the extent and pattern of intraarticular fractures in three dimensions. These imaging techniques combined with advances in methods of reducing and stabilizing intraarticular fractures have improved the ability of orthopaedists to restore the alignment and contour of fractured joint surfaces and led to an increase in the operative treatment of these injuries. However, available imaging techniques have limited ability to show disruption of articular cartilage that does not involve subchondral bone, and the value of current approaches to treatment of these injuries is uncertain.[74] There is no currently available method of assessing the extent of cell and matrix damage and there are no treatments for this type of articular surface damage. The extent and severity of these types of injuries may be important in determining the risk of progressive articular cartilage loss after intraarticular fractures; and, the existence of these injuries may help explain the variable results in patients with apparently similar intraarticular fractures that are treated by similar methods.

DISCUSSION

Limited understanding of the pathophysiology of synovial joint degeneration after injury makes it difficult to select

treatments that provide the best immediate restoration of function, and minimize the risks of developing posttraumatic OA and complications of treatment. The ability of joints in humans to recover from these injuries has not been studied rigorously, but in some instances, chondral repair tissue remodels and provides a functional articular surface. Animal experiments show that step-offs and gaps with a height or width comparable with that of the full-thickness of the articular cartilage have considerable potential for repair and remodeling and suggest that isolated articular surface defects of this degree do not substantially increase the risk of joint degeneration in stable normally aligned joints. The relationships between damage caused by acute injury and the effects of chronic increased articular contact stress caused by residual incongruity have not been defined and the biologic events responsible for progressive joint degeneration associated with either acute articular surface damage or chronic increased contact stress have not been elucidated. Furthermore, the relative contributions of posttraumatic residual articular surface incongruity and joint instability to the development of joint degeneration remain poorly understood. Joints vary in the risk of posttraumatic OA and age of the patient at the time of injury is an important risk factor. This information currently is not sufficient to allow selection of treatment that predictably minimizes the risk of progressive joint degeneration after joint injury.

There is a clear need for clinical and experimental studies of the relationship between joint injuries and joint degeneration and the mechanisms responsible for the joint degeneration that leads to posttraumatic OA. Development of clinically applicable methods of assessing cartilage cell and matrix damage, or at least reliably assessing the severity of articular surface damage, combined with increased understanding of the biologic events responsible for posttraumatic OA, will lead to better treatment of joint injuries. Without reliable accurate measures of the initial extent of tissue damage it is difficult to evaluate the efficacy of different treatments. Without understanding of the biologic events responsible for posttraumatic joint degeneration, it is difficult to devise effective methods of minimizing the tissue damage after injury and providing the optimal mechanical and biologic environment for joint repair and remodeling. Unanswered questions include: what biologic events cause joint degeneration after joint injury? To what extent is the risk of posttraumatic joint degeneration determined by the severity of the initial injury and the specific mechanical and biologic characteristics of the involved joint? Why does the risk of posttraumatic OA increase with age? What is the optimal biologic and mechanical environment to promote articular surface repair and remodeling? Answering these questions will provide a basis for better use of current treatments of joint injuries and development of improved methods of preventing and slowing the progression of posttraumatic OA.

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