

Mechanical Conditions That Accelerate Intervertebral Disc Degeneration: Overload *Versus* Immobilization

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Study Design. A review of the literature on macromechanical factors that accelerate disc degeneration with particular focus on distinguishing the roles of immobilization and overloading.

Objective. This review examines evidence from the literature in the areas of biomechanics, epidemiology, animal models, and intervertebral disc physiology. The purpose is to examine: 1) what are the degeneration-related alterations in structural, material, and failure properties in the disc; and 2) evidence in the literature for causal relationships between mechanical loading and alterations in those structural and material properties that constitute disc degeneration.

Summary of Background Data. It is widely assumed that the mechanical environment of the intervertebral disc at least in part determines its rate of degeneration. However, there are two plausible and contrasting theories as to the mechanical conditions that promote degeneration: 1) mechanical overload; and 2) reduced motion and loading.

Results. There are a greater number of studies addressing the “wear and tear” theory than the immobilization theory. Evidence is accumulating to support the notion that there is a “safe window” of tissue mechanical conditions in which the discs remain healthy.

Conclusions. It is concluded that probably any abnormal loading conditions (including overload and immobilization) can produce tissue trauma and/or adaptive changes that may result in disc degeneration. Adverse mechanical conditions can be due to external forces, or may result from impaired neuromuscular control of the paraspinal and abdominal muscles. Future studies will need to evaluate additional unquantified interactions between biomechanics and factors such as genetics and behavioral responses to pain and disability.

Key words: intervertebral disc, degeneration, biomechanics, immobilization, microfailure. **Spine** 2004;29:2724–2732

It is thought that the mechanical environment of the intervertebral disc can predispose to disc degeneration and associated painful symptoms. Disc degeneration appears to be an inevitable consequence of aging, with specific and substantial alterations occurring in the structural,

material, and failure properties of the disc over time. Despite this, aging and degeneration may involve separate processes, and there is wide variability in the extent to which the degenerative changes become painful and symptomatic. This paper examines the evidence concerning the relationship between mechanical environment and changes in the mechanical properties of the disc and its tissues as they relate to the pathogenesis of disc degeneration. In other words, what aspects of the mechanical environment of the disc accelerate degeneration, and what kind of mechanical environment inhibits degeneration? In particular, what are the relative roles of overloading and immobilization (or hypomobility) on the intervertebral disc?

In the context of this review, the two contrasting mechanical conditions (overload and immobilization) are terms used to imply alterations in both motion and loading. Intervertebral motion produces tissue strains, as does loading. An excessive range of motion will induce large strains of at least some of the spinal tissues. The converse may not necessarily be true, because lesser motion may not be a result of reduced loading. This review also concentrates on the macroscopic scale, although it is not possible to separate spinal behavior at this scale from the events at the cellular level.

■ Competing Hypotheses Concerning Which Mechanical Environments Accelerate Disc Degeneration

In the overload, or “wear and tear,” hypothesis, it is proposed that a demanding mechanical environment produces localized trauma of the disc that will be slow to heal because of the slow turnover of disc tissue.¹ Thus, the accumulation of tissue injury and “microtrauma” progressively weaken the disc, making it more susceptible to further injury (Figure 1). In this way, mechanical injuries weaken the disc, increasing the risk of further injury, and a vicious cycle of accumulating injury that outstrips the disc’s capability for biologic repair develops.^{2,3}

In a contrasting hypothesis for the mechanical pathogenesis of disc degeneration, it is suggested that hypomobility of the disc produces adaptive changes that may cause tissue weakness and degeneration, subsequent pain, and further reduced motion, again in a vicious cycle as was proposed for the case of articular cartilage.⁴ Within this hypothesis, there are differing explanations for the mechanisms of tissue weakening: hypomobility could produce altered (reduced) stimulus to the metabolic activity of disc cells (as reviewed by Setton in this issue of *Spine*) or altered transport of nutrients and metabolites (as reviewed by Urban in this issue of *Spine*). A

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of the spine that they control, each trunk loading condition can be associated with an indeterminate number of muscle activation patterns, each involving differing loads on the discs. Thus, there is no direct relationship between a task and the spinal loading—it depends on the individual and the individual circumstances. Coactivation of antagonistic muscles is apparently a strategy that increases trunk stability, but at the expense of added spinal loading.^{36–38} Increased spinal loading increases the segmental stiffness,^{39–43} and the additional stiffness can be a factor in increasing the stability of the spine.⁴³

Low back pain (LBP) is thought to be associated with altered muscle recruitment patterns, either as a predisposing cause of the pain or as a secondary response to pain. Three general aspects of altered muscle recruitment patterns in people with back pain have been investigated: 1) altered muscle activation patterns, especially coactivation, in a static task such as pulling against a fixed object or slow lifting; 2) altered muscle reflex latency times in response to a sudden perturbation such as a dropped weight, quick release of trunk loading, or moving support platform; and 3) altered muscle activation pattern in anticipation of an unexpected or voluntary perturbation.

The literature review by van Dieën *et al*⁴⁴ examined reports of trunk muscle activation with respect to two alternate hypotheses as to possible differences between patients with and without back pain. In the “pain-spasm-pain” hypothesis, it is proposed that a vicious cycle of hyperactivated muscles and pain develops, with the individual consciously or unconsciously “splinting” against painful motion. In the “pain adaptation” hypothesis, it is proposed that there is increased antagonistic activation of muscles that slows motion and hence guards against the exacerbation of existing pain. Their review indicated that the available data did not consistently support either hypothesis, and, as an alternative, the authors proposed that the observed differences were consistent with the notion that persons with back pain adopt strategies that enhance the stability of the spine.

■ Spinal Stability

Spinal instability is a term that has been used ambiguously to refer to intervertebral hypermobility, an altered pattern of intervertebral coupled motion, a variable pattern of painful symptoms, or frank buckling of the spinal column.⁴⁵ It is possible that sudden buckling of the spine is responsible for some sudden onset episodes of low back pain. Because the spine is inherently unstable, it must be stabilized by a combination of muscular and spinal stiffness.⁴³ In this supposed mechanism, spinal buckling causes large localized tissue deformations and associated painful tissue damage. Buckling instability cannot be induced experimentally in living patients, so it must be studied indirectly. For instance, after a perturbation, the amount of subsequent trunk excursion and/or the magnitude and timing of muscular response to a perturbation can be recorded. Persons with LBP

might respond differently to the anticipation of the perturbation or the actual perturbation. Two possible altered muscle activation strategies can be proposed: in the first, individuals with LBP would preactivate muscles to stiffen the trunk in anticipation (apprehension) of the perturbation, but at the cost of greater muscle forces and spinal loads, that might themselves be painful. In the second mechanism, they might be more likely to respond or possibly overactivate muscles following a perturbation, because they would be apprehensive of possibly large and painful tissue deformations.

■ Changes in the Mechanical Properties of the Spine as Correlated With Age and Degeneration

Motion Segments

In early stages of degeneration, the axial moment-rotation properties of the motion segment demonstrate some increases in range of motion, which are followed, in advanced degeneration, by some reduced range of motion and a tendency for the region of laxity around the “neutral position” to increase.⁴⁶ These findings are consistent with concepts of overload and hypomobility at early and later stages of degeneration, respectively.¹⁶ Flexion–extension and lateral bending, on the other hand, demonstrate a monotonic decrease in range of motion with the progression of degeneration.⁴⁶ These changes in the mechanical behavior may result from a combination of arthritic changes in the facet joints and subchondral sclerosis, though apparently independent of the presence of osteophytes.⁴⁷ However, the amount of variability between individual motion segments is large compared to the differences associated with degeneration.⁴⁸

In reality, the load displacement relationships in the intervertebral motion segments are highly complex and include six interrelated degrees of freedom, time-dependent behavior, and structural and material nonlinearity. These aspects may each be affected differently by degeneration. It has been proposed⁴⁹ that a region of laxity near the neutral position of a motion segment (the “neutral zone”) is most affected by degeneration and that this can lead to painful motion. The functional range of motion depends on spinal flexibility as well as the motion that is permitted by muscular control. Thus, although degeneration has been associated with motion segment hypermobility, pain is thought to restrict *in vivo* motion. However, many asymptomatic individuals also have a small *in vivo* range of spinal motion in the range considered to represent spinal impairment.⁵⁰ Trunk flexibility (*i.e.*, voluntary range of motion) is apparently not predictive of subsequent back pain.⁵¹

Intervertebral Disc

Degeneration and age-related changes in both the biochemical composition and structure of the anulus and nucleus of the intervertebral disc have been reported.^{52–56} As discs degenerate, the nucleus becomes more consolidated and fibrous and is less clearly demarcated

from the annulus fibrosus. Focal defects appear in the cartilage endplate, and there is a decrease in the number of layers of the annulus with an increase in the thickness and spacing of the collagen fibers.⁵⁷⁻⁵⁹ Degeneration is associated with decreased hydration, especially in the nucleus.⁵² Water content in the nucleus pulposus drops from about 90% of the tissue wet weight in the infant to less than 70% in the elderly. In the annulus fibrosus, the water content remains relatively constant with age and is approximately 60% to 70% of the tissue's wet weight.

As a consequence of these degeneration-related alterations in structure and composition (as reviewed by Roughley *et al* in this issue of *Spine*) of disc tissues, changes occur in material and structural properties of the component parts of the disc. The shear modulus of the nucleus increases 8-fold with degeneration and the decrease in relative energy dissipation suggests that the nucleus pulposus undergoes a transition from fluid-like to solid-like behavior with aging and degeneration.⁶⁰ In the annulus fibrosus, there is a significant increase in compressive modulus⁶¹ and decrease in radial permeability,⁶² as well as a moderate increase in shear modulus⁶³ of the tissue with grade of disc degeneration. These alterations may be explained by the loss of water content and increase in tissue density. Increases in the axial and circumferential permeability⁶² as well as alterations in the Poisson ratio⁶⁴ with degeneration are probably related to structural remodeling and perhaps microfailure resulting from the degenerative process. Alterations in the streaming potential response of annulus tissue with degeneration provide further evidence of the relationship between tissue fixed charge density, water content, and material properties.⁶⁵ These degeneration-related changes in material properties also correlate with age, making a distinction difficult because these two processes frequently occur in parallel. Separating these two effects may be a key step in understanding the process of disc degeneration.

These compositional and structural changes in turn alter the macroscopic behaviors as seen in the disc flexibility⁴⁶ and intradiscal pressure.^{12,66-68} Injurious joint loading conditions have mechanical consequences including fiber microfracture or macroscopic tissue failure.

Failure in Intervertebral Discs in Response to Loading

Evidence from *in vitro* motion segment testing including mechanical injury and fatigue experiments indicates that the disc can undergo tissue damage consistent with the formation of annular tears especially after sustained loading⁶⁹ and repetitive (fatiguing) loading¹⁹ intended to simulate a strenuous day's activity. The relative contributions of the annulus, nucleus, and posterior elements can be substantially altered by fluid shifts associated with sustained loading and by degenerative changes.^{66,70}

In vitro, lumbar disc rupture has been simulated through loading of the motion segment with hyperflexion and twisting and with fatigue loading.^{19,71,72} In fatigue loading, relatively modest magnitudes of repetitive flexion and extension as well as compression (to a lesser

extent) caused disc herniations in porcine spine motion segments.⁷³

Because the annulus can be considered to be a composite material, it is resistant to complete failure. The laminated structure of this kind of composite material requires multiple cracks and microfailure to occur (*i.e.*, matrix cracking, delaminations, and fiber failure) before final failure of the whole tissue. The annulus tissue can be damaged by a combination of fiber rupture and separation of layers (delamination). An evaluation of damage mechanisms in the disc annulus indicated that delaminations in the annulus are likely implicated in damage propagation, whereas fiber breaks were assumed to be a likely failure mode only under extreme loading conditions or when collagen damage occurs over a reasonably large region.⁷⁴ Delaminations have been reported as failure mechanisms for isolated annulus fibrosus specimens,⁷⁵ and separation of layers has been demonstrated in the annulus of intact motion segments.^{19,76,77} Delamination occurs in the presence of high interlaminar shear stresses that in turn are increased after initial radial and circumferential tears in the annulus.⁷⁸ The decrease in the number of layers and increase in the thickness of each layer that occurs with degeneration and aging⁵⁸ also directly increases the interlaminar shear stresses.⁷⁴

In studies of anatomic specimens, the presence of tears in the annulus fibrosus increases rotational (especially axial rotational) flexibility of lumbar motion segments⁷⁹ and is associated with disc degeneration.⁸⁰

A computational simulation of the disc degeneration process indicated that failure occurred initially at the endplates before annulus rupture and failure propagation.⁸¹ Failure at the endplate, such as a rim lesion, may initiate a stress free region or edge, thereby creating interlaminar shear stresses resulting in delamination and the initiation or propagation of failure in the annulus.^{74,78}

It is likely that mechanically induced remodeling leads, at least in part, to a causal relationship between altered kinematics and microfailure or macrofailure in the disc tissue leading to a degenerative cascade (Figure 1). Although the pathologic processes or the biomechanical disorders that give rise to disc degeneration and low back pain remain obscure,⁸² epidemiological studies point to a relationship. Physically fit people have a decreased incidence of low back pain, whereas sedentary posture is associated with back pain.^{20,82} Development of lumbar disc rupture is associated with activities generating higher disc stresses, including frequent bending and twisting, heavy physical work,²⁰ and exposure to vibration.⁸³ Two specific human conditions—spinal fusion and scoliosis—in which spinal loading is thought to be altered provide some insights into the possible link between mechanical environment and disc degeneration.

Clinical Evidence of Disc Degeneration in Fused Segments and Segments Adjacent to a Fusion

The apparently iatrogenic acceleration of degeneration in motion segments that are adjacent to a surgical arth-

rodosis (fusion) is often attributed to altered mechanics in the spinal column. The adjacent segments are assumed to experience altered biomechanical conditions, including increased intervertebral motion, facet loads, tissue stresses, and intradiscal pressure, which are affected by the length, location, and stiffness of the fusion mass^{84–91} supporting the overloading hypothesis. A decrease in the aggregating capacity of proteoglycans in the intervertebral disc, as well as a decrease in proteoglycan content in the nucleus, was reported at the fused level in a dog model.⁹² The authors further suggested that the biochemical differences at the fused levels were larger than those at adjacent segments but of similar nature.⁹²

Although a remodeling phenomenon is demonstrated in this animal model and may be at least partly responsible for a “degenerative cascade,” it is impossible to separate the concurrent degenerative disease processes from biomechanically induced changes in the case of human spinal fusion. This relationship is even less clear when symptomatic outcomes are considered, as adjacent segment degeneration may not produce clinical symptoms.^{93–96} It has also been suggested that individual characteristics such as genetics and psychosocial characteristics are more important than fusion length in predicting clinical outcome.^{97,98}

Disc Degeneration and Scoliosis

In human scoliosis, disc composition and ratio of type I to type II collagen is altered, with the total collagen concentration and ratio of type I to type II collagen being greatest on the concave side of the curve.⁹⁹ An elevated protein synthesis activity has also been observed in the convex side of scoliotic discs compared to the unaffected tissue.¹⁰⁰ These changes were attributed to altered mechanical environments in an expression of the Wolff Law. Other studies on scoliotic intervertebral discs further suggest that mechanical loading conditions lead to remodeling of the matrix proteoglycan content and structure, as well as expression of type X collagen.^{101–104}

In scoliotic discs removed at surgery, differences in cell viability correlated with changes in nutrient and metabolite levels and also with disc deformity (convex versus concave side, and distance from curve apex).¹⁰⁵ However, no loss of matrix macromolecules was seen in these studies. This was likely because the period between cell death and surgery was short compared to the long matrix turnover times. Intraoperatively (when the muscular loading of the spine was minimal), it was reported by Urban *et al*¹⁰⁶ that solute diffusion into the apical disc (measured by flux of nitrous oxide) was reduced. This could be due to abnormal mechanical stress on the disc or increased endplate calcification limiting solute diffusion.¹⁰⁶ The authors speculated that asymmetrical loads, tissue deformation, and nutrient supply may work separately or in combination to cause cell death within the disc. It appears that in scoliosis, there is a combination of overload and reduced motion that results in reported remodeling changes in composition and structure.

Alterations in Mechanical Loading in Animal Models and Tissue Culture

Numerous mechanical interventions to the disc *in vivo* have been shown to result in structural and compositional changes to the disc in animal models.¹⁰⁷ For example, in dogs, long distance running was shown to influence the proteoglycan content in the intervertebral discs, with reductions in the cervical and thoracic levels, but increases in the lumbar discs.¹⁰⁸ Compositional differences with spinal level were attributed to distinct biomechanical demands, suggesting that the type of mechanical forces, loading frequency, and duration all influence composition. Sustained superphysiological static compression on dog lumbar discs resulted in alterations in proteoglycan and collagen content and structure with no obvious signs of degeneration.^{109,110}

A number of animal models involving disc injury are reported, but here it is difficult to identify the contribution of alterations in mechanical environment of the tissue.^{40,111,112} The intended intervention may be confounded by reparative effects; for instance, in the Sullivan *et al* model,¹¹³ in which facet joints are removed from the rabbit lumbar spine with the intention of producing hypermobility, it was reported¹¹⁴ that a rapid formation (in a few weeks) of scar tissue resulted in the flexibility of the spine returning to preintervention values.

Mechanical interventions *in vivo* are more easily achieved in the tail than the spine, allowing more precise mechanical control over the joint loading conditions. Application of static loads on the order of 1 MPa have been shown to induce cell apoptosis and altered structural properties (disc thickness, axial compliance, and angular laxity), matrix content (proteoglycan and type I and II collagen), metalloproteinase activity, and disc cell gene expression (aggrecan and collagen II).^{115–119} This sustained axial compression resulted in a loss of disc height, altered disc stiffness, loss of water content, increased collagen fiber content in the nucleus, and cellular apoptosis with clear signs of degenerative changes. Historically, chronic load studies have focused on static compression applied 24 hours/day for 1 to 53 weeks.^{109,110,115–118} In a study that attempted to isolate immobilization from compression, a separate immobilization group of animals was used. Immobilization produced remodeling changes that were similar to static compression with lesser alterations in structure and composition.¹¹⁶ It is important to note, however, that 24 hours of static loading per day is not a physiologic loading condition, and even with separate immobilization groups, it is difficult or impossible to separate the effects of immobilization from altered loading. The tail models have also been criticized based on differences in loading (though not necessarily stress differences) between tail discs and spinal discs, and some differences in structural properties have been reported between discs of the tail and lumbar spine.¹²⁰

Recent device development has allowed investigation of the separate effects of immobilization and overloading in the *in vivo* tail models under dynamic conditions. It was demonstrated that dynamic compression results in

detectable alterations in gene expression and histochemistry within very short times (*i.e.*, 2 hours to 1 week).^{121,122} Notably, there was a threshold in both magnitude (~ 0.2 MPa) and frequency (~ 0.2 Hz) needed to maintain homeostasis in the disc.¹²³ Also, dropping below this threshold with immobilization loading resulted in a down-regulation of anabolic gene expression, whereas dynamic compression following immobilization resulted in a partial recovery of this down-regulation.¹²¹ Loading above this threshold with high compression magnitudes at either a high (1 Hz) or low frequency caused disc cells to respond by altering mRNA production.¹²³ This frequency threshold with dynamic compression loading was also reported for rat tail disc mechanical behaviors where daily 1-hour loadings at 0.7 MPa and 1.5 Hz for 17 days resulted in disc structural properties that were closest to the sham group with static compression and dynamic compression at 0.5 Hz and 2.5 Hz, resulting in more substantial alterations in structural properties.¹²⁴

The idea that activity increases the transport of nutrients and metabolites in the disc was investigated by Urban *et al.*¹²⁵ They reported that radioisotopes in the blood of exercising dogs were not transported into the disc at a rate faster than that expected by diffusion, suggesting that essential nutrients are transported through diffusion. However, they calculated that a “pumping” effect would augment transport of molecules larger than the sulfate ions in their experiments.

■ Mechanisms of Adaptive Changes in the Intervertebral Disc

Mechanically induced disc degeneration apparently occurs in two related pathways.⁶⁴ The first suggested pathway is that certain loading conditions directly damage the intervertebral disc, *e.g.*, hyperflexion^{72,81,90} The second (indirect mechanism) is that alterations in the material properties of disc subcomponents from damage or remodeling may weaken the disc. For example, mechanical stimuli may lead to loss of swelling pressure of the nucleus or decreased failure strength of the annulus fibrosus.^{60,61,63,64,126}

Although evidence on the metabolic responses of the disc to mechanical environment is being accumulated from cell, tissue, and organ culture studies, it remains difficult to identify the relationship between loading and degeneration at the macroscopic level. In cell and tissue culture, changes in hydrostatic pressure and osmotic pressure have been found to alter gene expression (TIMP-1, matrix metalloproteinase [MMP-3], types I and II collagen, aggrecan) and synthesis rates of extracellular matrix proteins (35S-sulfate and 3H-proline incorporation)^{127–131} in a dose-dependent and region-specific manner. It is interesting that static hydrostatic pressure applied to pieces of bovine discs for only 20 seconds (followed by 2 hours of recovery) tended to stimulate proteoglycan synthesis at low magnitudes (1–7.5 MPa), whereas 12 hours of loading resulted in an increase

in synthesis only at 5 MPa and a decrease at higher loads (7.5–10 MPa).¹³¹ Although it is very clear that intervertebral disc cells are quite sensitive to mechanical stimuli, the relationship between the joint loads applied to the intervertebral disc and its biologic response is not well understood.

Studies on the intervertebral disc tissue *in vitro* have attempted to isolate the precise biosynthetic response to applied mechanical loading. Compressive forces,¹³² vibration,¹³³ and pressurization^{127,128,130,131} stimulate proteoglycan and collagen production, yet at high magnitudes can inhibit protein production. The specific mechanical signals on disc cells include pressure, stress, and strain and can be evaluated with combined experimental and computational approaches.¹³⁴ These topics are addressed further in the review by Setton and Chen in this issue of *Spine*.

■ Conclusions Concerning Possible Mechanisms of Mechanically Accelerated Disc Degeneration

Evidence is accumulating to support the notion that there is a “safe window” of tissue mechanical conditions in which the discs remain healthy. Outside this range, overloading of the tissues produces localized injury that is slow to be repaired; conversely, a mechanical environment that is deprived of motion and other mechanical stimulus impairs the maintenance of tissue homeostasis. Thus, both situations can lead to disc degeneration. Muscular forces form the largest contribution to spinal loading under most circumstances, so differing neuromuscular control may help to explain why some individuals are more susceptible to degeneration that is secondary to inappropriate mechanical loading. Because both immobilization and overloading are implicated in remodeling of the disc, it is likely that both can contribute to progressive degeneration. However, it appears that more studies have been directed at documenting the effects of “wear and tear” and overload than the effects of underuse and immobilization. *In vivo* studies of patients with LBP demonstrate reduced intervertebral motion and increases in compression and shear loading on the spine in certain activities. *In vivo* animal models with controlled compression loading have documented the effects of immobilization and overloading separately and show that there is a threshold of mechanical loading required for maintaining normal (“healthy”) disc composition, structure, and mechanical properties. Immobilization leads to reduced protein synthesis that may result from a lack of mechanical stimulus (or stimulus below a certain threshold) or lack of nutritional supply. On the other hand, according to animal studies, high magnitudes and high frequencies of dynamic and static compression produce cell apoptosis, increased catabolic gene expression and enzymatic activity, and altered structural properties.

The causal relationship between mechanical loading and degenerative changes in the human spine are less

clear. It is likely, however, that disc remodeling in response to immobilization or overload may result in altered (and perhaps deteriorated) material properties and changes in structure, and this may predispose the disc to failure on the microstructural or macrostructural level. However, mechanical studies on the tissue level and motion segment level also indicate that disc ruptures and their progression in a “degenerative cascade” can only occur when overloading is also involved.

■ Key Points

- The majority of studies on mechanical involvement in disc degeneration focus on the “wear and tear theory” and not on the influence of underuse and immobilization.
- Mechanical studies on the tissue level and motion segment level indicate that disc ruptures and their progression in a “degenerative cascade” can only occur when overloading is also involved.
- Both immobilization and overloading are implicated in remodeling of the disc. Overloading of the tissues produces localized injury that is slow to be repaired, whereas a mechanical environment that is deprived of motion and other mechanical stimuli also impairs the maintenance of tissue homeostasis.

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