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Mechanical Initiation of Intervertebral Disc Degeneration

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Study Design. Mechanical testing of cadaveric lumbar motion segments.

Objectives. To test the hypothesis that minor damage to a vertebral body can lead to progressive disruption of the adjacent intervertebral disc.

Summary of Background Data. Disc degeneration involves gross structural disruption as well as cell-mediated changes in matrix composition, but there is little evidence concerning which comes first. Comparatively minor damage to a vertebral body is known to decompress the adjacent discs, and this may adversely affect both structure and cell function in the disc.

Methods. In this study, 38 cadaveric lumbar motion segments (mean age, 51 years) were subjected to complex mechanical loading to simulate typical activities *in vivo* while the distribution of compressive stress in the disc matrix was measured using a pressure transducer mounted in a needle 1.3 mm in diameter. "Stress profiles" were repeated after a controlled compressive overload injury had reduced motion segment height by approximately 1%. Moderate repetitive loading, appropriate for the simulation of light manual labor, then was applied to the damaged specimens for approximately 4 hours, and stress profilometry was repeated a third time. Discs then were sectioned and photographed.

Results. Endplate damage reduced pressure in the adjacent nucleus pulposus by 25% ± 27% and generated peaks of compressive stress in the anulus, usually posteriorly to the nucleus. Discs 50 to 70 years of age were affected the most. Repetitive loading further decompressed the nucleus and intensified stress concentrations in the anulus, especially in simulated lordotic postures. Sagittal plane sections of 15 of the discs showed an inwardly collapsing anulus in 9 discs, extreme outward bulging of the anulus in 11 discs, and complete radial fissures in 2 discs, 1 of which allowed posterior migration of nucleus pulposus. Comparisons with the results from tissue culture experiments indicated that the observed changes in matrix compressive stress would inhibit disc cell metabolism throughout the disc, and could lead to progressive deterioration of the matrix.

Conclusions. Minor damage to a vertebral body endplate leads to progressive structural changes in the adjacent intervertebral discs. [Key words: biomechanics, cadaver testing, compression, degeneration, endplate fracture, intervertebral disc] **Spine 2000;25:1625–1636**

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Recent pain provocation studies have confirmed that severe and chronic back pain can be reproduced by mechanical stimulation of degenerated intervertebral discs.[50,59,74] Magnetic resonance imaging (MRI) and discographic studies, however, show poor correspondence between generalized disc degeneration and back pain, suggesting that only certain features of degenerated discs are likely to be painful, such as a radial fissure in the anulus fibrosus[60] or posterior disc protrusion.[18] Other "degenerative" changes such as a loss of signal intensity from the nucleus may be only signs of aging.[83] Also, degenerative changes may become less painful as they become more severe because disc narrowing can cause the disc to be protected from mechanical loading by the adjacent apophyseal joints.[12,31] Despite these complications, there is no doubt that disc degeneration can be painful, yet surprisingly little is known about it.

Even defining disc degeneration is difficult. Degeneration involves biologic (cell-mediated) changes, which are most pronounced in the nucleus,[8,26,66,81] and gross structural changes, which are most evident in the anulus and endplate.[5,26,41,81] Common structural changes include radial fissures, circumferential clefts and rim tears in the anulus,[81] inward buckling of the inner anulus,[36,77] increased radial bulging of the anulus, reduced disc height, endplate defects, and vertical bulging of the endplates into the adjacent vertebral bodies.

A less common but clinically important structural change is herniation of nucleus pulposus through the anulus or endplate. Changes in the discs often are accompanied by arthritic changes in the apophyseal joints, and by osteophytes around the margins of the vertebral bodies.[81] Disc function deteriorates along with its structure: A healthy disc contains a soft and highly hydrated central region, the nucleus pulposus, which acts as a hydraulic cushion to distribute stress evenly between vertebrae, whereas degenerated discs have only a small hydrostatic region, or none, and exhibit high stress concentrations in the anulus.[5,12]

Traditionally, disc degeneration has been linked to mechanical loading, although direct postmortem confirmation of this is relatively recent.[85] Gross structural disruption certainly appears to represent mechanical failure, but tissue composition often is changed as well, and it is not clear whether discs fail mechanically because they are weakened by biochemical changes, or whether the latter represent a cellular response to mechanical failure. The importance of mechanical factors in disc degeneration is emphasized by experiments on cadaver spines,

which show that disc prolapse and radial fissures can be simulated in apparently normal discs if the loading is sufficiently severe[7,57] or relentless,[6,32,76] and by animal experiments showing that biologic degeneration always occurs after scalpel-induced structural failure.[69,72]

The issue is far from settled, however, because epidemiologic studies on identical twins suggest that inheritance is the largest single determinant of disc degeneration,[16] and this inheritance is at least partly genetic in nature.[84] There may be genetic weaknesses in the collagen framework of the disc or genetic influences on blood supply and disc metabolism.[84] Equally, genetic susceptibility may involve mechanical factors such as small discs, a heavy torso, or small internal levers, which would lead to high internal muscle forces acting on the disc.

The problem of whether disc degeneration usually is initiated by mechanical or biologic factors is important because it affects strategies of research on the prevention and treatment of disc-related back pain. Currently, there is considerable interest in identifying biochemical and metabolic abnormalities in degenerated disc tissues,[27,35,45,46,66] but these abnormalities may be consequences of disc failure rather than causes, and the precise sequence of biologic events after some mechanical disruption may offer little opportunity for intervention. Similarly, efforts to measure and regulate spinal loading[29] may be of little use in preventing back pain if primary biochemical factors can predispose discs to fail under low loads. Cause and effect is difficult to establish because any biochemical weakening would lead directly to mechanical disruption, and mechanical disruption would influence disc cell metabolism immediately through its effect on matrix compressive stress.[13,38,42]

One way of tackling this problem of cause and effect is to uncouple the close links between mechanical and biologic factors and study one factor in isolation. Experiments on cadaver spines performed over a few hours enable cell-mediated events to be ignored so mechanical factors that might initiate disc degeneration can be studied in detail. If cadaver experiments could show that physiologically reasonable mechanical loading can consistently create all of the commonly observed structural changes that typify disc degeneration, this would add weight to the "mechanics first" argument. The argument would be strengthened further if the mechanically induced structural changes could be shown to alter the matrix compressive stresses in a manner that would be expected to inhibit disc cell metabolism.

Previous cadaver experiments have demonstrated that disc herniation,[7,57] radial fissures,[6,32] and posterior disc bulging[4,7] can be caused by severe or repetitive mechanical loading of apparently normal discs, but several problems remain. No explanation exists for the types of internal disruption that occur in the lamellar structure of the anulus,[28,36,77,80] which are more common than disc prolapse. Also, it is difficult to explain how mechanical loading could cause disc degeneration in sedentary people who recall no preceding injury. A possible solution to both problems was suggested by a recent study from the laboratory of the current authors,[13] which showed that even slight mechanical damage to the weakest link of the lumbar spine, the vertebral body endplate, affected stress distributions in the adjacent disc in a manner that could lead to internal disruption of the disc. Fatigue damage to the endplates can occur at loads well within the normal range of spinal loading in life.[19,39]

The purpose of the current study was to extend the previous experiment of the authors and test the hypothesis that minor damage to a vertebral body can lead to progressive disruption of the adjacent disc.

■ Materials and Methods

Overview of Experiments. In this study, 38 cadaveric lumbar "motion segments" were used in three experiments. The first experiment compared the severity of endplate damage with changes in the distribution of compressive stress in the adjacent disc. It also sought to identify which discs were affected most by endplate damage. The second experiment investigated how affected discs would respond to subsequent cyclic loading: Would it cause a redistribution of fluid in the disc and a consequent equalization of stress, or would it intensify the stress concentrations caused by endplate damage? The third experiment examined the ability of discs to equalize compressive stress in flexed and lordotic "postures," both before and after endplate damage.

After testing, the discs were sectioned and photographed so structural changes caused by mechanical loading could be compared with those that typify degenerated discs. Changes in the distribution of matrix compressive stress were interpreted in the light of recent experiments on disc tissue metabolism to infer the likely response of disc cells to the structural defects created by mechanical loading.

Cadaver Material. Cadaveric lumbar spines were obtained from individuals whose cause of death was unrelated to spinal pathology. These were stored in sealed plastic bags at −20 C for up to 6 months. Spines were radiographed to exclude any that exhibited such advanced disc degeneration (including gross narrowing and bridging osteophytes) that dissection and testing would have been difficult.

In the experiments, 19 spines, 19 to 87 years of age, were used. When needed for testing, each spine was defrosted at 3 C in its sealed bag and then dissected into two "motion segments" consisting of two complete lumbar vertebrae and the intervening disc and ligaments. One motion segment was tested immediately. The other was resealed in a bag, stored at 3 C, and tested the next day. The following levels were represented: L5–S1 (2 motion segments), L4–L5 (13 motion segments), L3–L4 (4 motion segments), L2–L3 (12 motion segments), L1–L2 (4 motion segments), and T12–L1 (3 motion segments). Of these motion segments, 30 were male and 8 were female. The mean age of the 38 motion segments was 51 ± 16 years.

Mechanical Testing. Each motion segment was secured in two cups of mildly exothermic dental plaster and tested on a computer-controlled hydraulic materials testing machine (Dartec, Stourbridge, UK). Complex loading in bending and compression was applied by means of two low-friction rollers (Figure 1). When the rollers were of equal height, the specimen was subjected to pure compression. When the rear roller was

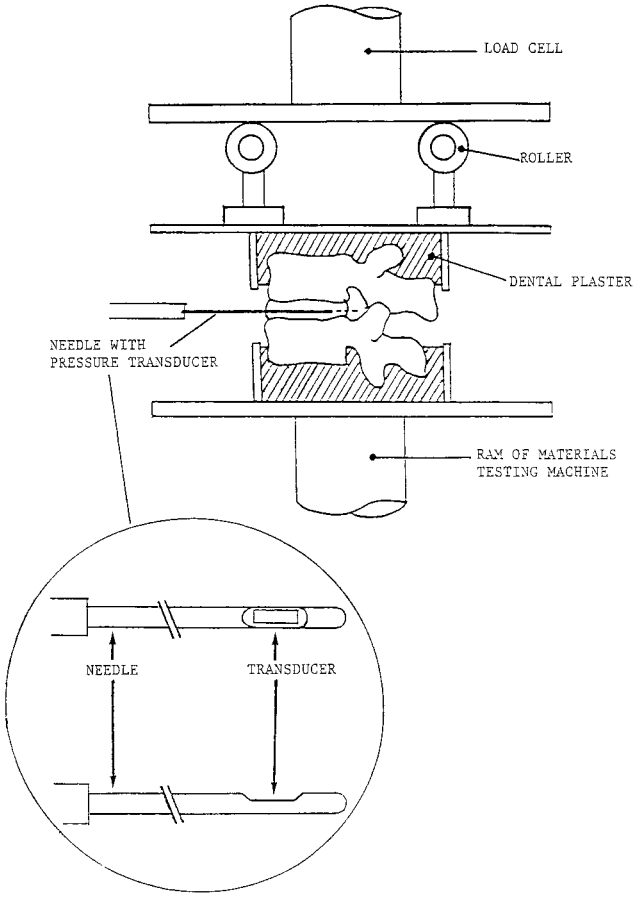

Figure 1. Lumbar motion segments were secured in cups of dental plaster and loaded on a servo-controlled materials testing machine. Two rollers maintained a constant angle between vertebrae when compressive loads were applied. Specimens could be positioned in flexion or extension by varying the height of the rear roller. The distribution of matrix compressive stress was measured by pulling a pressure transducer through the disc along its mid-sagittal diameter.

lower, the specimen was loaded initially in bending by the front roller, and thus flexed forward until the rear roller made contact with the load-cell plate. The specimen then was loaded in compression and bending. The apparatus did not impose any axis of flexion–extension, but allowed small "settling" movements in the horizontal plane while high complex loading was applied at physiologic loading rates. Throughout the testing period, the disc was surrounded with cling-film to keep its surface moist. In this way, the swelling pressure of the disc was able to oppose the load-induced outflow of fluid.

Preliminary Creep Test. Each motion segment was subjected to a pure compressive force of 300 N for approximately 15 minutes as a precaution against any postmortem superhydration effects. This force was sufficient to cause an approximate 0.1 to 0.2-mm loss in disc height, with the result that the disc approached (but did not reach) equilibrium with the 300 N. In life, the lumbar spine is subjected to approximately 200 N during each night's rest, and 500 N during relaxed standing.[63]

Measurement of Intradiscal Compressive Stress. A static compressive load of 2 kN, sufficient to simulate light manual labor,[63] was applied to the motion segment for a period of 20 seconds. During this time, the distribution of compressive stress in the disc was measured at a frequency of 25 Hz by pulling a miniature pressure transducer through it, along its sagittal midline, as shown in Figure 1. The transducer was a small strain-gauged membrane mounted in the side of a needle 1.3 mm in diameter.[58] The anulus has excellent self-sealing properties,[6,52] so no disc material was expressed through the needle hole during the experiments. Validation tests have shown that the output of the transducer in disc tissues is approximately equal to the average compressive stress acting perpendicularly to the membrane.[55] Rotating the needle about its long axis enabled the vertical and horizontal components of compressive stress to be measured in successive tests using the same needle track.

Each pair of "stress profiles" was analyzed as described previously[12] for the purpose of calculating the following: the width of the hydrostatic nucleus (expressed as a percentage of the anteroposterior diameter of the disc), the average pressure in the nucleus, and the peak stress (horizontal or vertical) in the anterior anulus and the posterior anulus regions of the profiles. Peak vertical stresses usually were greater than peak horizontal stresses.[12] The hydrostatic nucleus was defined as that region of the profile in which the vertical and horizontal stresses did not differ from each other or vary with location by more than 5%.

■ Damage to the Vertebral Endplate

After the initial stress profilometry, each motion segment was positioned in moderate flexion to simulate the flat back adopted when ordinary people lift weights from the ground.[29,30] Flexion angles reflected the mobility of each motion segment, and thus ranged from 4° for elderly upper-lumbar motion segments to 8° for young lower lumbar motion segments. A compressive overload injury then was simulated as follows: The ram of the Dartec moved upward at approximately 2.5 mm/second until the first signs of damage were evidenced by a slight reduction in gradient of the force-deformation graph, which was plotted in real time.[13] The load then was removed immediately. Damage was confirmed by compressing the specimen a second time and noting the residual displacement from the force-displacement graphs. The damage was quantified by measuring residual displacement at a compressive force of 1 kN. Because this measure shows the permanent loss of motion segment height resulting from mechanical overload, it is a better measure of damage than that used previously in the authors' laboratory.[13] Compressive damage occurs in the vertebral body endplate rather than the disc,[19,20,25,71] and might occur in life during a fall on the buttocks, or by the process of fatigue failure during repetitive strenuous lifting. Endplate damage sustained by sudden compressive overload *in vitro* is similar to that resulting from cyclic loading,[19,20] but is more convenient to reproduce in the laboratory. Approximately 5 minutes elapsed between the last stress profile measured before endplate damage and the first measured after the damage.

Experiment 1. All 38 specimens were used. After the preliminary 15-minute creep test, stress profiles were obtained with the motion segment positioned in the neutral position (0°), which involves neither flexion nor extension. Next, the endplate was damaged as described earlier and stress profilometry repeated. Changes in the stress profiles were compared with the following specimen characteristics: age, lumbar level, and height loss (*i.e.*, severity of damage).

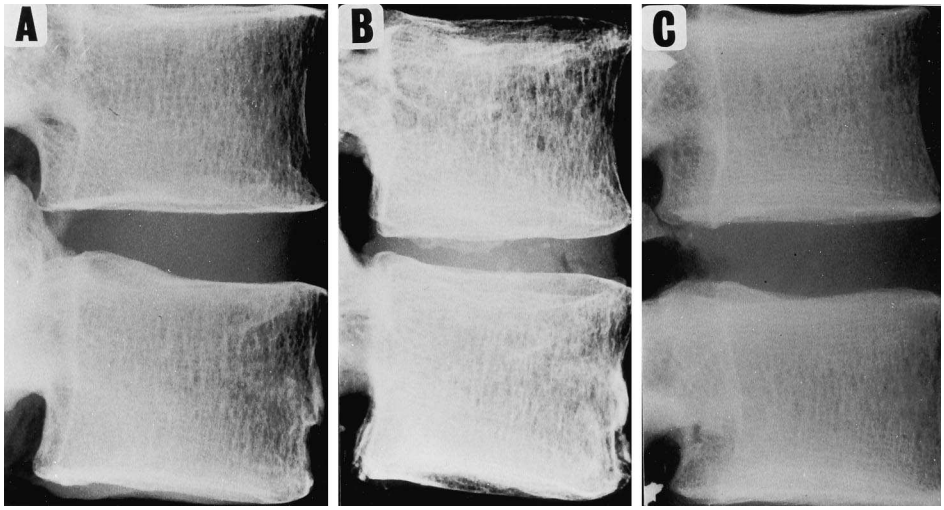

Figure 2. Radiographs of a typical motion segment both before (**A**) and after (**B**) endplate damage and cyclic loading. Specimen = M-61 L23. Note the concave endplates in **B.** Young specimens (**C**) often showed only slight radiographic signs of damage after testing (M-21 L23). This specimen had lost 1.3 mm in height.

Experiment 2. After the endplate had been damaged, 19 of the specimens used in Experiment 1 were subjected to cyclic compressive loading. The last to be tested, these 19 specimens were not selected in any other way. Nine motion segments were positioned in moderate flexion (4–8°) to simulate a "flat back," and 10 motion segments were positioned in 2° of extension to simulate lordotic standing postures.[4] Between 8000 and 10,000 linear, 1.5-second ramp loading/unloading cycles were applied under "load control." The minimum compressive force during each cycle was approximately 50 N, and the maximum was in the range of 1.5 to 3 kN (mean, 2.2 kN), depending on specimen size and age. This is appropriate to the simulation of moderately light manual labor.[63] Stress profilometry was repeated a third time immediately after cyclic loading.

Experiment 3. The influence of "posture" on the 19 motion segments in experiment 2 was examined by repeating the stress profilometry in 2° of extension and 4° to 8° of flexion. Stress profiles were obtained in these two postures and the neutral posture (0°) before and after endplate damage, than again after cyclic loading.

Examination of Disc Structural Damage. Immediately after testing, 15 of the 19 specimens in Experiments 2 and 3 were frozen at −80° and subsequently sectioned in the sagittal plane for the purpose of visualizing any disruption in the lamellar structure of the anulus fibrosus. The disc and half of the adjacent vertebral bodies were cut from each frozen motion segment. This vertebral body–disc–vertebral body unit then was cut into parasagittal sections 5 mm thick, using a saw to cut through bone and a sharp knife to cut through frozen disc tissue. Sections were photographed under low-angle incident light to allow individual lamellae of the anulus to be visualized.

Two of the authors (M.A., P.D.) assessed the slides independently for the following features: inward (reverse) bulging of the inner lamellae (midsagittal slices only) and outward bulging of the outer lamellae beyond the farthest rim of the vertebral body. Bulging was quantified by dividing the maximum horizontal displacement of a lamella's path by the vertical distance between its end points. Features were considered as present only if both authors noted them independently. It was not possible to assess control (unloaded) discs in a similar manner because all available motion segments were tested, and the intervening discs were cut in the horizontal plane during initial dissection.

The remaining 23 discs were sectioned in the horizontal plane for comparison with discs tested previously in the authors' laboratory.[6,7] The precise nature of the endplate damage was not investigated because this would have required defatting procedures, which would have interfered with the investigations of the disc. The nature of endplate damage in cadaver specimens subjected to compressive overload has been investigated thoroughly by others.[20]

Statistical Methods. Matched-pair *t* tests were used to examine differences in intradiscal stress distributions at various stages of the experiments. One-tailed tests were used because the direction of changes could be anticipated from previous work.[11–13,56] Single and multiple linear regression procedures were used to test for the dependence of intradiscal stresses on continuous variables such as age and damage severity. Differences cited later were all highly significant ($P < 0.005$) unless stated otherwise.

■ Results

Experiment 1

Compressive damage occurred at 6.7 ± 2.5 kN (range, 3–11.6 kN), resulting in a permanent height loss of 0.72 ± 0.39 mm (range, 0.17–2.11 mm), which is equivalent to approximately 1% of motion segment height (Figure 2). Subsequent sectioning showed that compressive failure involved cracking of a vertebral endplate, the trabeculae supporting it, or both, sometimes accompanied by a vertical displacement of some nucleus pulposus into the vertebral body, as described previously.[13,19,20,71] One specimen failed by a posterior prolapse of the disc. It is unusual, but not rare, for discs to herniate in this way while positioned in only moderate flexion, provided the compressive force is very high.[7]

Compressive damage caused an average fall of 25% ± 27% in nucleus pressure, and an average reduction of 25% ± 26% in the maximum vertical or horizontal compressive stress in the anterior anulus (Figure 3). Maximum stresses in the posterior anulus, however, increased by 16% ± 49% ($P = 0.014$). The height of stress "peaks" in the anulus were defined relative to the pressure in the nucleus: In the posterior anulus, these peaks increased by 191%, from 0.45 MPa to 1.31MPa, after vertebral damage. The anteroposterior diameter of the hydrostatic nucleus decreased from 53% to 40% after vertebral damage. The lateral diameter of the nucleus presumably decreased also, although stress profiles were not measured in this direction.

The fall in nucleus pressure depended on the severity of vertebral damage, as indicated by specimen height loss (Figure 4). Nucleus decompression also was more marked in discs 50 to 70 years of age (Figure 5). No significant correlation was found between damage severity and age, and multiple regression showed that the dependence of nucleus decompression on age remained significant after correction for damage severity ($P = 0.007$). Lumbar level had no significant effect on nucleus decompression. The height increase of stress peaks in the posterior anulus after vertebral damage was proportional to the fall in nucleus pressure ($R = 0.40$; $P = 0.014$). Figure 6 shows how vertebral damage greatly affected a typical middle-age disc but had comparatively little effect on a young disc.

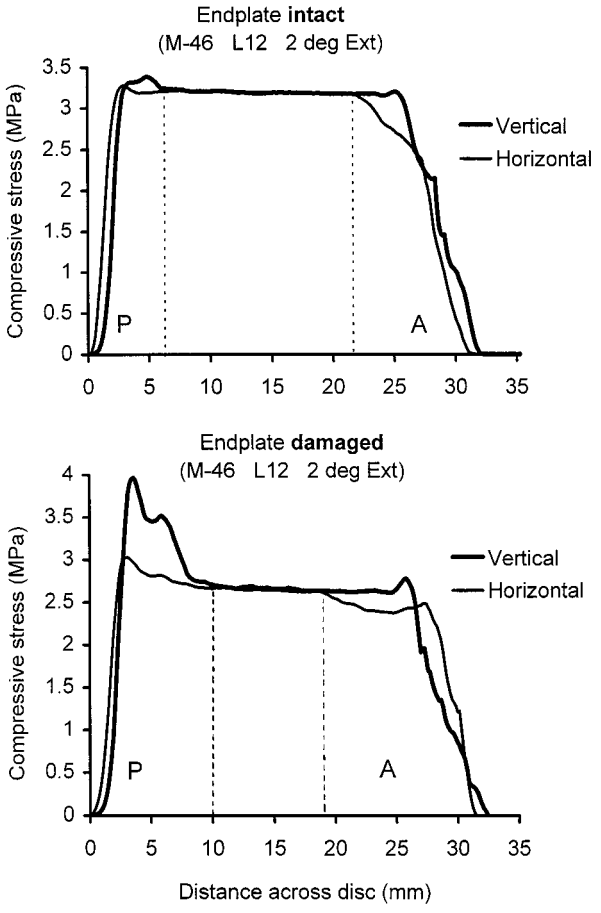

Figure 3. The effects of endplate damage on the distribution of matrix compressive stress along the anteroposterior (A-P) diameter of the adjacent disc. Typically, endplate damage reduced the size of the region with hydrostatic properties (shown by the dotted lines), reduced the pressure in this region, and generated high peaks of compressive stress in the anulus fibrosus. These stress distributions were taken with the motion segment positioned in 2° of extension to simulate the erect standing posture.

Experiment 2

Cyclic loading did not equalize stress distributions by causing loose tissue to migrate from regions of high stress to regions of low stress. On the contrary, it made the stress peaks worse (Figure 7). Average results for the 19 discs tested in the neutral posture showed that vertebral damage decreased nucleus pressure from 1.76 to 1.41 MPa, and cyclic loading decreased it further to 1.23 MPa (Table 1, Column 2). Cyclic loading also decreased the diameter of the hydrostatic nucleus, from 40% to 30% of the anteroposterior diameter ($P = 0.015$). It also increased the small stress peaks in the anterior anulus from 0.08 to 0.20 MPa ($P = 0.015$). Stress peaks in the posterior anulus increased from 1.31 to 1.45 MPa, but this failed to reach significance ($P = 0.18$).

Experiment 3

The effects of endplate damage and subsequent cyclic loading were particularly large in lordotic postures: In 2° extension, stress peaks in the posterior anulus increased from 0.60 to 1.91MPa, and the fall in nucleus pressure was greater than in the neutral posture (Table 1). Flexion, however, reduced the posterior stress peaks and tended to even up the maximum stresses in the anterior and posterior anuli at all stages of the experiment. Even after damage and cyclic loading, moderate flexion was able to restore an approximately normal distribution of compressive stress across most discs. Table 1 summarizes

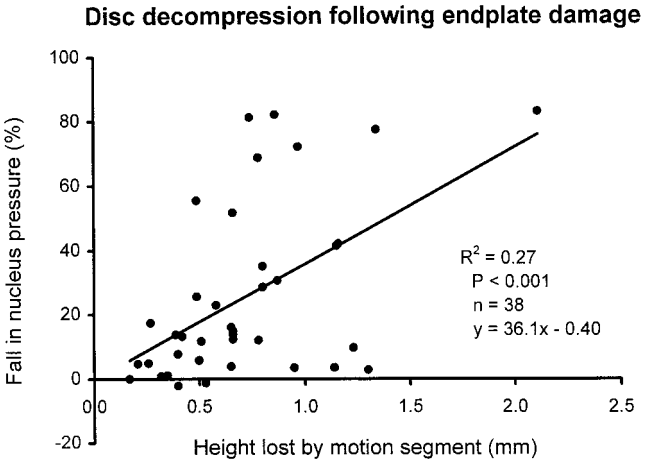

Figure 4. Vertebral endplate damage reduced the pressure in the nucleus pulposus of adjacent discs. Disc decompression increased significantly ($P < 0.001$) with the extent of the damage, as indicated by the height lost permanently by the motion segment.

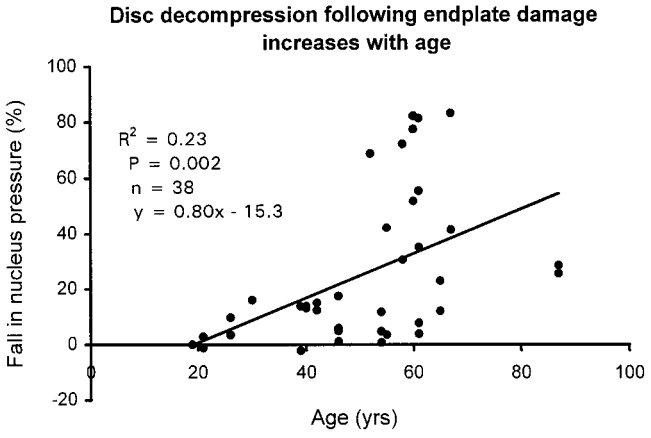

Figure 5. The fall in pressure in the nucleus pulposus after vertebral endplate damage was significantly greater in older specimens ($P < 0.002$). The pressure was greatest in specimens 50 to 70 years of age.

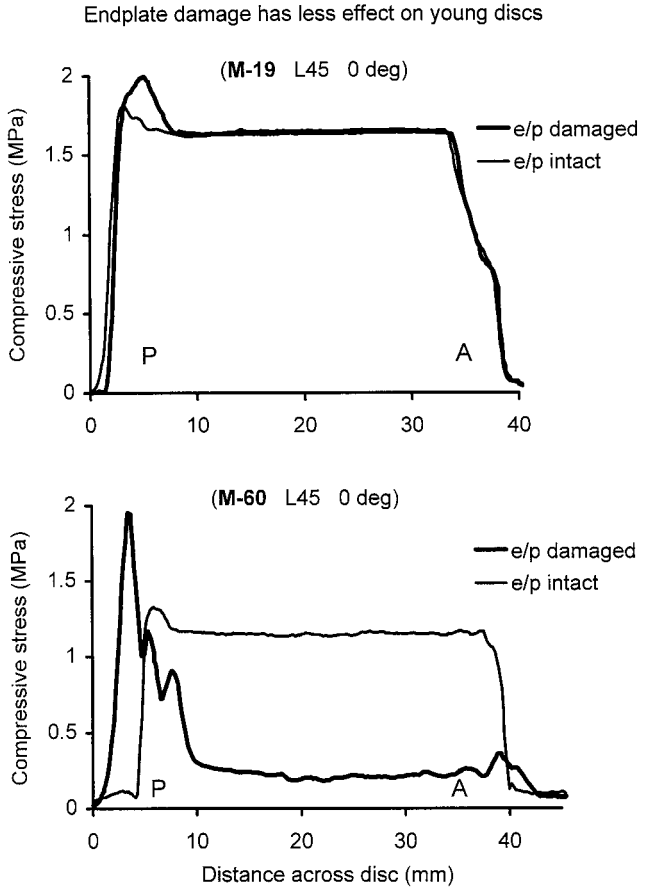

Figure 6. Endplate damage in young specimens often had only a slight effect on the adjacent discs (upper). However, some middle-age discs were severely affected (lower). The dramatic decompression of this 60-year-old disc probably is accompanied by increased loading of the apophyseal joints after disc height loss. The profiles suggest that posterior bulging of the anulus increases after endplate damage. For clarity, only vertical compressive stresses are shown.

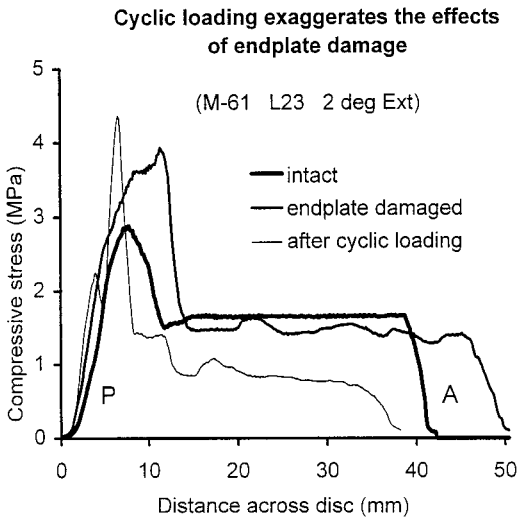

Figure 7. In this typical disc, endplate damage increased both the stress peak in the posterior anulus and the apparent width of the whole disc, presumably by causing more radial bulging of the anterior anulus. Cyclic loading intensified the stress peak in the posterior anulus, further decompressed the nucleus, and unloaded the anterior anulus. These stress distributions were taken with the motion segment positioned in 2° of extension to simulate the erect standing posture. This may have led to stress-shielding of the disc by the apophyseal joints after cyclic loading. For clarity, only vertical compressive stresses are shown.

the effects of endplate damage and cyclic loading on intradiscal stresses in the three postures examined.

Structural Damage in the Discs

Sagittal plane disc sections indicated inward bulging of the anterior anulus in 8 of 15 discs, and of the posterior anulus in 9 of 15 discs (Figure 8). Usually, the same discs were affected anteriorly and posteriorly, and it was most apparent in the middle-age discs that had the most greatly altered stress profiles. Outward bulging of the outer anulus beyond the farthest margins of the vertebral body rim was observed anteriorly in 8 of 15 discs, and posteriorly in 14 of 15 discs. In 11 of these 14 discs, the "hairpin" bulging of the posterior lamellae was so pronounced that the horizontal displacement of the lamellae exceeded their vertical height.

Surprisingly, the patterns of structural disruption showed no significant dependence on whether the cyclic loading had been in flexion or extension. Two discs (not including the disc that prolapsed when overloaded in compression; Figure 9A) showed complete radial fissures in the posterior anulus, and in one of these discs, it appeared that some nucleus pulposus had migrated down the fissure during the period of cyclic loading (Figure 9B). Horizontal sectioning of the remaining 23 discs showed that the anulus often portrayed the bell-shaped deformations reported previously.[6]

■ Discussion

These experiments showed that minor compressive damage to a middle-age lumbar vertebra sufficient to reduce

Table 1. Effects of Endplate Damage and Subsequent Cyclic Loading on the Distribution of Compressive Stress Inside Lumbar Intervertebral Discs

	Maximum Stress in Region of Disc					
	Post A (MPa)	Nuc (MPa)	Ant A (MPa)	Width Of Nucleus (%)	Post A Peaks (MPa)	Ant A Peaks (MPa)
Intact						
Extension (−2°)	2.31	1.72	1.86	47	0.60	0.14
	(0.66)	(0.59)	(0.67)	(15)	(0.50)	(0.23)
Neutral (0°)	2.22	1.76	1.90	53	0.45	0.14
	(0.72)	(0.54)	(0.62)	(14)	(0.39)	(0.24)
Flat back (4–8°)	2.31	1.86	2.33	46	0.45	0.47
	(0.87)	(0.66)	(0.88)	(19)	(0.37)	(0.73)
Endplate damaged						
Extension (−2°)	2.95	1.29	1.40	37	1.66	0.11
	(1.14)	(0.69)	(0.82)	(17)	(1.23)	(0.31)
Neutral (0°)	2.72	1.41	1.49	40	1.31	0.08
	(0.88)	(0.67)	(0.71)	(18)	(1.02)	(0.21)
Flat back (4–8°)	2.04	1.50	1.94	39	0.54	0.44
	(0.77)	(0.53)	(0.73)	(22)	(0.62)	(0.67)
After cyclic loading						
Extension (−2°)	2.98	1.07	1.26	26	1.91	0.19
	(1.34)	(0.66)	(0.83)	(20)	(1.20)	(0.41)
Neutral (0°)	2.68	1.23	1.44	30	1.45	0.20
	(1.11)	(0.67)	(0.80)	(21)	(1.31)	(0.32)
Flat back (4–8°)	1.98	1.38	2.02	38	0.60	0.64
	(0.59)	(0.46)	(0.45)	(21)	(0.53)	(0.48)

Values shown are the mean (standard deviation) values for 19 discs. Post A = maximum stress in the posterior anulus, Ant A = maximum stress in the anterior anulus, Nuc = mean pressure in the nucleus. Also shown are the width of the hydrostatic nucleus pulposus (expressed as a percentage of the full anteroposterior diameter of the disc) and the size of stress "peaks" in the posterior anulus (relative to nucleus pressure). Note that endplate damage decompresses the nucleus and increases the stress peaks in the posterior anulus. Cyclic loading exaggerates these effects.

motion segment height by approximately 1% causes large and progressive changes in the internal stress distribution of adjacent intervertebral discs. Additional evidence suggested that during subsequent cyclic loading, the lamellae of the anulus could buckle in toward the nucleus, or outward beyond the edge of the vertebral body, and that the disrupted lamellae could allow migration of nucleus pulposus material.

The latter inferences were not supported by observations on control (unloaded) discs, so there is no proof that the lamellae in these discs were not disrupted before testing began. However, previous postmortem studies have reported that inwardly collapsing lamellae become common only in elderly discs,[36,77] whereas more than half of the discs in the current study were affected, although most were younger than 60 years of age. Also, the fact that the abnormalities in stress distributions were made worse by the cyclic loading rather than better suggested that a progressive mechanical failure had been initiated in the discs.

The underlying mechanism of internal disc disruption is probably as follows: The damaged endplate deforms more when under load,[22] allowing more space for the hydrated nucleus pulposus, or allowing some nucleus tissue to pass through it. The nucleus therefore experiences a reduction in pressure,[23] which is similar in amount to the reduction seen in degenerated discs.[12,64] The decompressed disc bulges more and loses height.[24] This process is intensified by water loss after sustained loading.[10] Less of the applied compressive force is resisted by the decompressed nucleus, so more must be resisted by the surrounding anulus (and apophyseal joints). High stress gradients in the anulus then force the inner lamellae inward toward the decompressed nucleus[75] and the outer lamellae outward. The buckling of the lamellae is encouraged by the accompanying loss in disc height.

The effects are greater in older discs because their tissues are less hydrated, and therefore less able to deform sufficiently to reduce steep stress gradients. Nucleus pulposus material can move into the disrupted anulus during repetitive loading, but bulk extrusion of nucleus pulposus from the disc (Figure 9A) can be achieved (*in vitro*) only if the motion segment is heavily loaded in flexion or hyperflexion.[7,25,57] If endplate damage has similar consequences in living people, then a mechanical explanation exists for the typical structural features of disc degeneration.

The validity of cadaveric experiments was considered in detail previously.[2] It was concluded that the extremely low cell density, and metabolic rate of human discs, and the relatively small effects of frozen storage on motion segment mechanics[70] and intradiscal pressure[65] enable the results of short-term mechanical experiments to be extrapolated to living people with some confidence. Evidence that frozen storage affects disc water content[43] or creep properties[14] may be attributable to artifactual swelling of freeze-thawed discs after removal of the ligamentum flavum, which normally prestresses the disc.[54] Any postmortem changes in disc hydration must be small

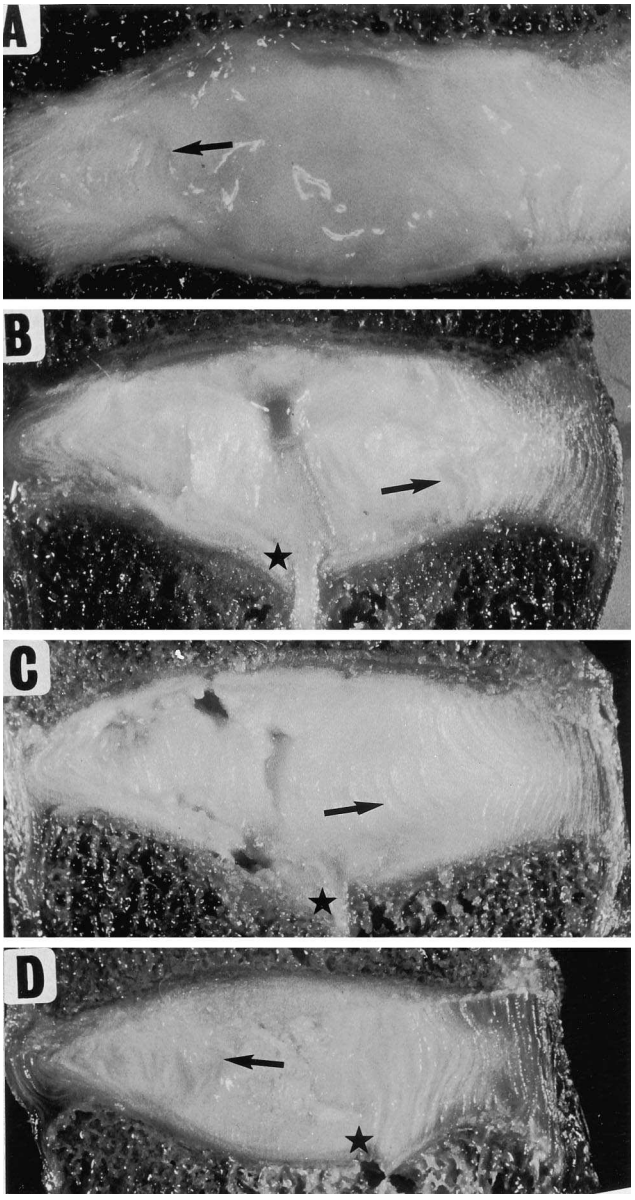

Figure 8. Midsagittal sections of intervertebral discs after endplate fracture and cyclic loading. **A** = M-19 L45; **B** = M-42 L45; **C** = M-42 L23, **D** = F-61 L45. Note the inward bulging of the inner anulus lamellae (arrows) and the extreme outward bulging of the outer lamellae. Damage to the vertebral body endplate is visible on some sections (*).

because hydration naturally varies by 20% during the course of each day, and a similar variation is observed in cadaver discs subjected to prolonged physiologic creep loading.[54] Freezing appears to cause some permanent change in pig discs,[14] which have a water content of 90%, but this may not apply to less hydrated human discs. Apparent changes in the creep properties of discs immediately after death[47] are caused, at least in part, by the poor reproducibility of the measurements even before death.[1] Diurnal fluid flow *in vivo* may prevent fatigue damage from accumulating as quickly as in cadaver experiments, but this possibility has not been investigated. The complex loading of discs in life, which comes from gravity and muscle attachments, can be simulated in cadaveric experiments by summing all of the relevant forces into one "resultant" force, provided its magnitude, direction, and point of application are chosen appropriately.[9] The only assumptions required are quite justifiable,[2] so there appears to be no reason why cadaver experiments should not be used to simulate short-term mechanical changes in living discs.

In the longer term, however, mechanical events would be accompanied by biologic events, as disc cells respond to changes in their mechanical environment. Tissue culture experiments show that abnormally high and abnormally low hydrostatic pressures both inhibit disc cell metabolism,[38,42] and that pressures of 3 MPa can stimulate the production of the matrix-degrading enzyme MMP3.[38]

In the current experiments, structural disruption to the endplate and anulus reduced the ability of the disc to distribute compressive stresses evenly, especially in lordotic postures, so regions of very high and very low stress were generated. A large pressure drop in the nucleus pulposus (Figure 6, lower) would inhibit cells in the nucleus from synthesizing more proteoglycans and restoring the volume of the nucleus. On the contrary, nucleus volume, and therefore pressure, probably would fall even more, exacerbating the short-term effects simulated in the current experiments. In the anulus, peak stresses often exceeded 3 MPa, and these would be expected to inhibit disc cell metabolism and hinder attempts to repair the collagen network. Therefore, by destroying the disc's ability to equalize compressive stress, structural failure would inhibit matrix synthesis permanently and progressively in both nucleus and anulus. A relatively minor injury to a vertebral body, which might quickly heal, then would leave a progressive long-term problem for the adjacent discs. Endplate damage also could lead to disc degeneration by other means: for example, by hindering metabolite transport from the vertebral body into the nucleus,[53] or by instigating an inflammatory[35,68,80] or autoimmune[17] reaction in the disc or the vertebral body.[78]

There is plenty of circumstantial evidence linking endplate damage with disc degeneration. According to Vernon-Roberts,[81] discs with Schmorl's nodes tend to exhibit advanced degenerative changes at an earlier age, and the earliest changes are sometimes adjacent to the endplate defect. In a large MRI study, Hamanichi et al[37] showed that Schmorl's nodes were present in 19% of patients with back or leg pain, as compared with 9% of controls. These authors found Schmorl's nodes to be particularly common in patients ages 10 to 39 years, and 60 to 69 years. The nodes often were associated with posterior disc prolapse, especially at the lower lumbar levels. It is possible that long-term biochemical changes may render old Schmorl's nodes "invisible" to MRI scans in later life.

Schmorl's nodes at more than one level were a frequent finding.[37] In young people, they were associated with vigorous sports, suggesting that they may be caused by an impulsive force acting up the spine. The fact that Schmorl's nodes in young people often are of little clini-

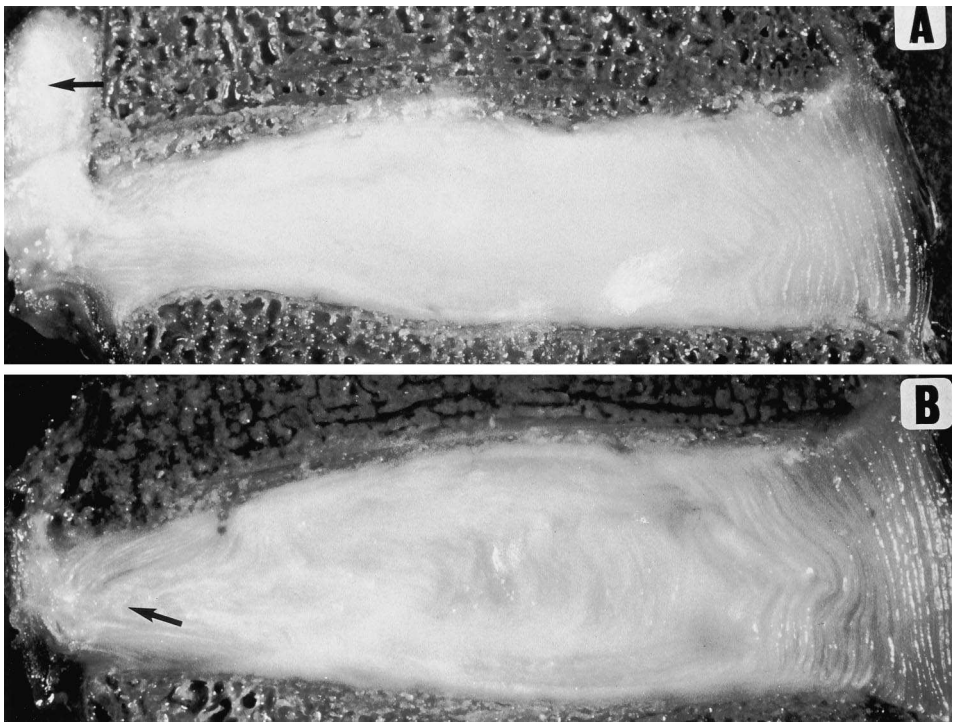

Figure 9. Midsagittal sections of intervertebral discs after testing. **A,** Posterior herniation of nucleus pulposus occurred suddenly at a flexion angle of 6° and a compressive force of 9.8 kN (specimen M-40 L23). The extruded fragment of nucleus (arrow) was trapped behind the posterior longitudinal ligament. It did not appear to increase in size during cyclic loading (according to observations of the motion segment), possibly because the nucleus was decompressed. **B,** This specimen failed in the vertebral body, but after cyclic loading, a complete radial fissure was noted in the posterior anulus (arrow). Very little nucleus pulposus was extruded through the fissure (specimen M-40 L45).

cal relevance may be explained by the increased ability of young discs to equalize compressive stress after endplate damage (Figure 6). Associations between recently occurring endplate damage in middle-age people and subsequent disc degeneration have yet to be explored.

The mechanical initiation of disc degeneration suggested by the current study complements previous biochemical and histologic investigations of disc aging and degeneration. Biochemical aging, which begins at birth, is manifested by increasing fragmentation and loss of proteoglycans,[26] water loss,[8] brown pigmentation,[66] and changes in matrix collagens.[66] These changes occur earlier and to a greater extent in the nucleus than in the anulus, and they may be attributable to "oxidative stress" arising from nutritional compromise.[66,67] In contrast, the types of structural disruption studied in the current experiment tend to appear later, usually after the age of 20 years, and they affect primarily the anulus and endplate.[66,81] Moreover, in adults, disc herniation and endplate defects show little correlation with age,[83] and they most commonly affect only the lower lumbar levels. It therefore appears that structural disruption of discs should not be viewed simply as a more-or-less inevitable extension of age-related changes.

In combination, the biochemical and biomechanical evidence suggests that disc "degeneration" represents some mechanical, or possibly nutritional, injury superimposed on normal tissue aging. It may be significant that Type I collagen, associated with tissues subjected to nonhydrostatic stresses, appears in the nucleus pulposus only after the age when gross structural damage is common.[66] This again suggests that mechanical events drive the biochemical changes because a marked reduction in the size of the hydrostatic nucleus was seen after the structural disruption produced in the current experiments (Table 1) whereas little change in nucleus size followed (creep-induced) loss of water from the disc.[10]

The relative importance of metabolic and mechanical "injuries" as initiators of disc degeneration is difficult to determine because they interact with each other and with genetic inheritance. For example, cigarette smoking, which probably impairs metabolite transport into the discs, increases the risk of disc degeneration,[15] but some of this small risk may be attributable to genetic inheritance and shared early environment in families of smokers rather than to the cigarette smoke itself.[15,16] Nevertheless, the fact that structural degenerative changes are much more common in the lower lumbar discs than in the upper discs,[83] although they would have similar nutritional problems, suggests that nutritional "injuries" are less important than mechanical injuries.

Regular physical activity appears to reduce or increase the risks of disc degeneration, depending on how severe it is. This complication probably is caused by the ability of skeletal tissues to strengthen with regular moderate exercise[51] but to experience (fatigue) failure if the loading is too severe.[86] "Adaptive remodeling" in response to controlled exercise explains why professional tennis players have 30% more bone in their racquet arm,[44] and why physically active individuals have extremely strong vertebrae[33,34] and discs.[73] Conversely, a lack of exercise leads to tissue weakening, and this may explain why some sedentary occupations increase the risk of disc prolapse.[49] The weakened spinal tissues would be vulnerable to accidental injury during slips and falls.

Intervertebral discs may be particularly vulnerable to injury and fatigue damage when they are subjected to sudden and large increases in mechanical loading because increased physical loading will strengthen muscles and bones faster than the avascular discs.[3] These considerations could explain why the highest known risk factors for disc prolapse involve the frequent lifting of heavy loads, either at work[49] or in the home,[61] although some manual occupations carry no greater risk than sedentary work.[48]

The mechanisms discussed earlier suggest how disc degeneration might be initiated by structural disruption to the vertebral endplate. However, is there biomechanical evidence to show that many people overload their backs sufficiently to damage their vertebrae? In postmenopausal women and elderly men, high forces are not always necessary to cause endplate fractures: Many are reported to occur during everyday activities, as shown in a recent review by Myers.[62] In younger people, a single overload injury could be caused by a fall on the buttocks, or by a maximal contraction of the trunk muscles during exceptional circumstances.

Vertebrae can be crushed by muscle action during epileptic seizures,[79] and a similar lack of muscle inhibition may occur during alarming incidents,[87] or in the heat of sporting competition. Like other muscles, the erector spinae are strongest when contracting eccentrically. They can generate particularly high forces when preventing forced flexion of the trunk. During repetitive activities, muscle action undoubtedly can lead to fatigue failure of the vertebral endplate: *In vitro,* there is a 70% risk of failure at approximately 40% to 50% of the specimen's normal compressive failure load if 5000 loading cycles are applied,[19] which is only 3 to 4 kN for average young men.[20,71] For comparison, the peak compressive force on the spine rises to approximately 4.4 kN when weights of 20 kg are lifted from the ground.[29] It appears that only the adaptive remodeling process prevents all workers in heavy manual jobs from sustaining fatigue damage to their vertebrae, and the likelihood of an individual being injured will depend on metabolic factors as much as the rigors of the job. Not surprisingly, minor defects to the vertebral body endplate or to its supporting trabeculae are very common,[21,40,82] and may explain why endplates become more concave with increasing age.[21]

The aforementioned evidence explains how high or repetitive compressive loading might initiate lumbar disc degeneration. Other explanations are possible, such as hyperflexion injury[7] or defects in the vitamin D receptor gene,[84] and it reasonable to suppose that several factors may contribute to disc degeneration in individual cases. However, repetitive mechanical loading may prove to be the factor that can be controlled most easily. Effective control does not simply mean minimizing spinal loading, because that would lead to weak backs that are vulnerable to accidents. Manual handling legislation should recognize that mechanical and metabolic risks interact, so that too little physical exertion may be as harmful as too much. Also, mechanical risk factors themselves can be environmental or genetic, so a given work activity may harm one back but strengthen another. Links between disc degeneration and back pain also are complicated, as discussed in the introductory paragraphs. However, it would be unfortunate if mechanical explanations of disc degeneration and back pain were abandoned simply because they are not as simple as was first supposed.

■ Conclusions

Minor compressive damage to the vertebral body endplate alters the distribution of matrix compressive stress in the adjacent intervertebral disc. The nucleus is decompressed, and stress peaks appear in the anulus. Discs 50 to 70 years of age are affected most, presumably because they have a reduced capacity to deform and equalize compressive stress.

Subsequent loading does not reverse the changes in intradiscal stress. It makes them worse. Repetitive loading after endplate damage appears to cause buckling of the lamellae of the anulus: The inner lamellae can collapse inward and the outer lamellae bulge outward, particularly in the posterior anulus. Nucleus pulposus tissue can migrate into and through the disrupted lamellae.

In life, the altered matrix stresses would be expected to inhibit disc cell metabolism, so that a progressive biologic reaction to the structural disruption would occur.

■ Key Points

- Intervertebral disc degeneration involves structural disruption and cell-mediated changes in composition, but it is not clear which comes first.
- This experiment on cadaveric lumbar motion segments showed that compressive damage to the vertebral body endplate alters the distribution of matrix compressive stress in the adjacent intervertebral disc. The nucleus is decompressed, and stress peaks appear in the anulus.
- Subsequent cyclic loading made these changes worse, and there was some evidence to suggest that the anulus was collapsing gradually into the decompressed nucleus.
- Previous tissue culture experiments suggest that the altered stress distributions would adversely affect disc cell metabolism.

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