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Current Understanding of Lumbar Intervertebral Disc Degeneration: A Review With Emphasis Upon Etiology, Pathophysiology, and Lumbar Magnetic Resonance Imaging Findings

The lumbar intervertebral discs (IVDs) are of critical importance for the support and mobility of the spine.[16,54,71] These remarkable tissues have the capacity to maintain stability under a wide variety of loading conditions, while still permitting intersegmental motion.[7,16] Unfortunately, the lumbar IVDs undergo more destructive changes over a lifetime than do any other musculoskeletal tissues[53] and often contribute directly, or indirectly, to the symptoms of low back pain and sciatica.[61,62,90,91]

Although abnormalities of the lumbar IVD can manifest in many different ways, such as bulging or herniation, the common central feature to most disc pathology is the process of specific degenerative changes that occurs within the nucleus, annulus, and adjacent bony tissue.[5,8,98] This complex process of cell-mediated structural changes occurs over a lifespan, with signs of disc degeneration (DD) often present by the third decade of life, and almost universal by the seventh and eighth decades.[18,44,51,53] Not surprisingly, DD is the most common condition affecting the adult spine and is the reason for over 90% of all adult spinal surgeries.[8]

SUPPLEMENTAL VIDEOS ONLINE

• **SYNOPSIS:** Degeneration of the lumbar intervertebral discs (IVDs) is highly prevalent in adults and nearly universal in the elderly population. Degenerative changes within, and adjacent to, the IVDs are likely to contribute to a variety of pain syndromes; however, the exact association between these findings and symptoms remains speculative. Recent research has provided new information regarding the etiology, pathophysiology, and clinical relevance of degeneration of the IVD. This information will assist clinicians and researchers in understanding the development and clinical course of lumbar disc degeneration, as well as its potential impact upon patients seeking physical therapy care for back pain. The purposes of this clinical commentary are to review the structure and metabolic capacity of the normal and degenerative lumbar IVD, and to discuss factors that influence the onset and progression of disc degeneration. Lumbar magnetic resonance images will be used to illustrate the common findings associated with this condition.

• **LEVEL OF EVIDENCE:** Diagnosis, level 5.
J Orthop Sports Phys Ther 2008;38(6):329-340. doi:10.2519/jospt.2008.2768

• **KEY WORDS:** *back pain, lumbar disc, MRI, rehabilitation*

Although exact data are lacking, it is quite likely that a high percentage of adults seeking physical therapy care for low back pain and/or sciatica will have imaging evidence of lumbar DD at 1 or more spinal levels. The exact role that these findings play in symptom generation is, however, often unknown. For example, several population-based or case control studies have also reported a high prevalence of DD in asymptomatic people.[19,57,97] This has led to a lack of consensus regarding the importance of the presence of DD relative to determining patient prognosis and treatment.

Over the past several years, a growing body of evidence has provided valuable information regarding the etiology of lumbar DD[6,13,50,105,116] and the pathophysiology of the degenerative lumbar IVD.[5,27,58,70,94,99,101] This information will assist clinicians and researchers in understanding the development and clinical course of lumbar DD and its potential impact upon patients seeking physical therapy care for back pain. The purposes of this clinical commentary are to review

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the structure and metabolic capacity of the normal and degenerative lumbar IVD, and to discuss factors that influence the onset and progression of DD. Lumbar magnetic resonance images (MRIs) will be used to illustrate the common findings associated with this condition.

THE NORMAL LUMBAR INTERVERTEBRAL DISC

Structural Components

The healthy IVD is composed of a series of concentrically arranged layers of fibrocartilage that surround and restrain an amorphous, well-hydrated, inner core of proteoglycan gel.[16,54,71] Strongly bound to the vertebral bodies and cartilaginous vertebral endplates, the composite make-up of the IVD creates a hydraulic system that can absorb and transmit various combinations of compression, shear, and tensile forces.[4,5,55] In addition, the healthy disc creates a "spacer effect"; that is, it maintains sufficient vertical distance between the vertebrae (disc height) to provide ligamentous tension, alignment of the facet joints, and adequate space for the passage of neurovascular structures within the vertebral foramina.[16]

Traditionally, the lumbar IVD has been described as consisting of 2 primary layers: the annulus fibrosus and the nucleus pulposus. It has been suggested, however, that describing the IVD from the perspective of 4 concentrically arranged tissue layers that occur in tandem with one another would provide a better understanding of the distinct morphologic and biochemical characteristics that contribute to DD[54,60] (**FIGURE 1**).

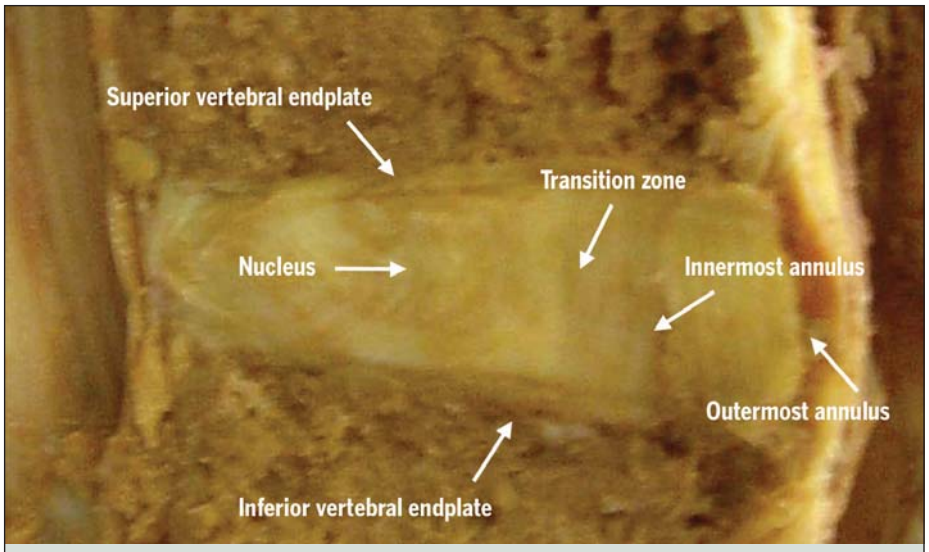

FIGURE 1. A midsagittal dissection of an L4-5 intervertebral disc (IVD) in a cadaveric specimen obtained from a 63-year-old male. This specimen illustrates the 4 regions of the IVD as well as the superior and inferior vertebral endplates. Note the anterior (right) and posterior (left) longitudinal ligaments that encompass the anterior and posterior surfaces of the IVD.

The 4 Tissue Layers

The First Layer The outermost annulus provides substantial resistance to tensile loads. To achieve this, the outermost layer consists of dense, well-orientated type I collagen fibers arranged in a lamellar configuration.[5,16] These fibers are strongly bound to the periphery of the vertebral body and to the outer margins of the end plate. The anterior and posterior longitudinal ligaments reinforce this layer, providing additional stability.

It is in this relatively thin, outermost layer of the annulus and its adjacent longitudinal ligaments that virtually all of the neurovascular structures within the IVD are located.[16,34,35] In the normal IVD the sensory nerve fibers[16,35,88] and their accompanying blood vessels[112] are most dense posteriorly and anterior-laterally but are generally observed only to a depth of 3.5 mm from the periphery of the annulus. Interestingly, sensory information from these nerves travels in the sinuvertebral nerve to the spinal cord via 2 possible routes: segmentally through the adjacent dorsal root or extrasegmentally through the paravertebral sympathetic chain.[34,110] This dual pattern of sensory information is thought to contribute to the often diffuse spatial location of pain symptoms associated with IVD impairment.[110,111]

The Second Layer The inner portion of the annulus also contains thick, type I collagen fibers, but they lack the parallel organization of the outermost annulus.[54] As they approach the center of the IVD, these fibers have gradually less dense arrangements and differentiate into the transitional zone.

The Third Layer The transitional zone is composed of thin, fibrous tissue that borders and encompasses the fourth and deepest layer, the nucleus pulposus.

The Fourth Layer The nucleus pulposus is a gel-like region composed mainly of water that is held in suspension by the hydrophilic properties of glygosaminoglycans (chondroitin and keratin sulfate), which are bonded to proteoglycan molecules.[16,48,54] In contrast to the dense outermost layer of the annulus, the nucleus pulposus is loosely bound together with irregularly arranged elastin and thin, type II collagen.[5] The differences between the well hydrated nuclear region and its less hydrated adjacent structures are illustrated by MRIs that are weighted to highlight the "T_2-features" of these tissues.[14] The variations in signal intensity (brightness) of T_2-weighted images demonstrate the contrast between tissues based upon their relative fluid content. Tissues with a high fluid concentration, such as the normal nucleus pulposus, result in a high (bright) T_2-signal, whereas those structures with a relatively low fluid concentration, such as the annular region, give off a low (dark) T_2-signal (**FIGURE 2**).

The vertebral endplate is a critical structure bordering the IVD. This large,

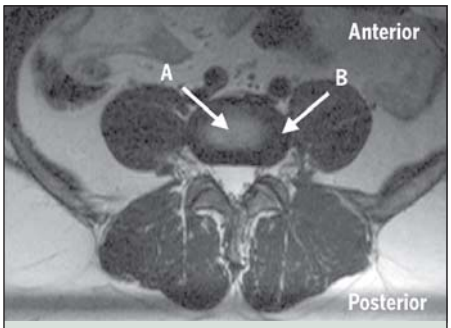

FIGURE 2. An axial T_2-weighted image of a normal L5-S1 intervertebral disc (IVD). Note the high (bright) signal generated from the nuclear region (arrow A) and the low (dark) signal from the annular region (arrow B).

flat plate of cartilage ranges in thickness from 0.1 to 1.6 mm and spans the central portions of the superior and inferior vertebral bodies to act as a semipermeable barrier between the subchondral bone of the vertebral body and the IVD (**FIGURE 1**).[16,54,71,81,101,104] The portion of the endplate adjacent to the IVD is primarily composed of fibrocartilage and strongly bound to the nuclear and annular regions. However, the portion adjacent to the vertebral body is primarily composed of hyaline cartilage that is weakly attached to subchondral bone, creating a "weak link" when the IVDs are exposed to trauma.[71,81]

Nutritional Capacity of the Healthy Disc

Homeostasis is maintained within the IVD by cellular activities that act to regulate the synthesis and turnover of extracellular components, such as collagen and proteoglycans.[16,22,58,107,113] The outermost layer of the annulus contains a small number of cells, the majority of which are fibrocytes that secrete type I collagen. The nuclear region of the IVD primarily contains chondrocytes that secrete proteoglycans and type II collagen.[5,58]

Optimal cellular activity requires a steady supply of oxygen and nutrients to support the aerobic metabolism needed to synthesize collagen and proteoglycans.[53,70,114] Additionally, metabolic end products, such as lactate, must be removed. In vascularized tissues, these processes are achieved by blood flow; however, because the adult IVD is largely avascular, it must rely upon diffusion for the transport of small molecules and bulk fluid flow for the transport of larger molecules into and out of the disc.[5,36,70,104] The distance that these molecules must travel can be quite long. Because the blood supply within the IVD is limited to the outer annular region, the nearest blood supply to the majority of disc tissues in an adult is located in the subchondral regions of the vertebral bodies. This may be as far as 20 mm from the center of the disc.[101] Considering the distances that need to be traveled, the exchange of nutrients in the IVD via diffusion and bulk flow can be challenging; this requires the molecules of interest to extravasate out of the capillaries in the subchondral bone, across the vertebral endplate, and travel within the extracellular matrix to the target cells of interest.[36] Metabolic waste must reverse this process to be removed. A recent study using gadolinium-enhanced lumbar MRI to track diffusion reported that, in healthy discs, the process of "diffusion march" from the vertebral body to the center of the IVD took 2 hours to cross the endplate, and 4 more hours to show substantial increase in the center of the IVD.[101]

The rate of tissue-fluid exchange within the disc is mediated by electrochemical events and is influenced by the presence or absence of tissue barriers, such as the vertebral endplate[104] and fibrous tissues near and within the IVD (sometimes called "nuclear clefts").[79] Strong negative charges exerted by proteoglycans act to attract and bind water.[16] However, proteoglycan activity can be influenced by the nature of spinal loading and unloading.[4,5,31,55,70,99,113] This is thought to account for the large variation in compressive strength of the nucleus that ranges from approximately 2.8 to 13.0 kN (630-2900 lb).[5] In addition, loading and unloading the spine creates mechanical gradients that may also influence the magnitude of tissue-fluid exchange.[37,55] This is illustrated by diurnal variations in the signal intensity of the nuclear region of T_2-weighted MRI. In healthy, young discs the signal intensity representing hydration is higher (indicating a greater water concentration) in the morning after several hours of recumbency, and is lower in the evening after several hours of upright loading.[2,17,60,75,89,103] Boos et al[17] reported an average height loss of 0.9 mm per disc over the course of the day in healthy young adults, and Roberts et al[103] found a mean increase in total body height of 19.3 mm and a mean increase in disc volume of 1300 mm^3 in healthy, young females following recumbency. Karakida et al[60] reported similar findings for normal discs in young people. However, degenerative discs and normal discs in people over 35 years of age did not exhibit measurable diurnal variations. The absence of detectable diurnal variations in degenerative and aged discs is consistent with the findings of Rajasekaran et al,[101] which supports the hypothesis that a decreased ability to perform fluid exchange is an important component of DD.

INTERVERTEBRAL DISC DEGENERATION

Overview

The term *disc degeneration* encompasses a wide array of morphologic and biochemical descriptions that can involve specific regions within the IVD or its entire structure. In recent work, Adams and Roughley[5] have proposed that the most meaningful definition of DD should be, "an aberrant, cell-mediated response to progressive structural failure." This can be conceptualized as follows: the hydraulic mechanism necessary to absorb and transmit loads through the IVD is based upon the hydration of the nucleus and the structural stability of the surrounding structures (the inner and outermost annulus and the vertebral endplate).[4,5,16,54] In this mechanism, the nucleus acts to reduce stress on the vertebral endplate and the surrounding structures act as a restraining mechanism of the nucleus. Intact discs spread loads evenly; however, any

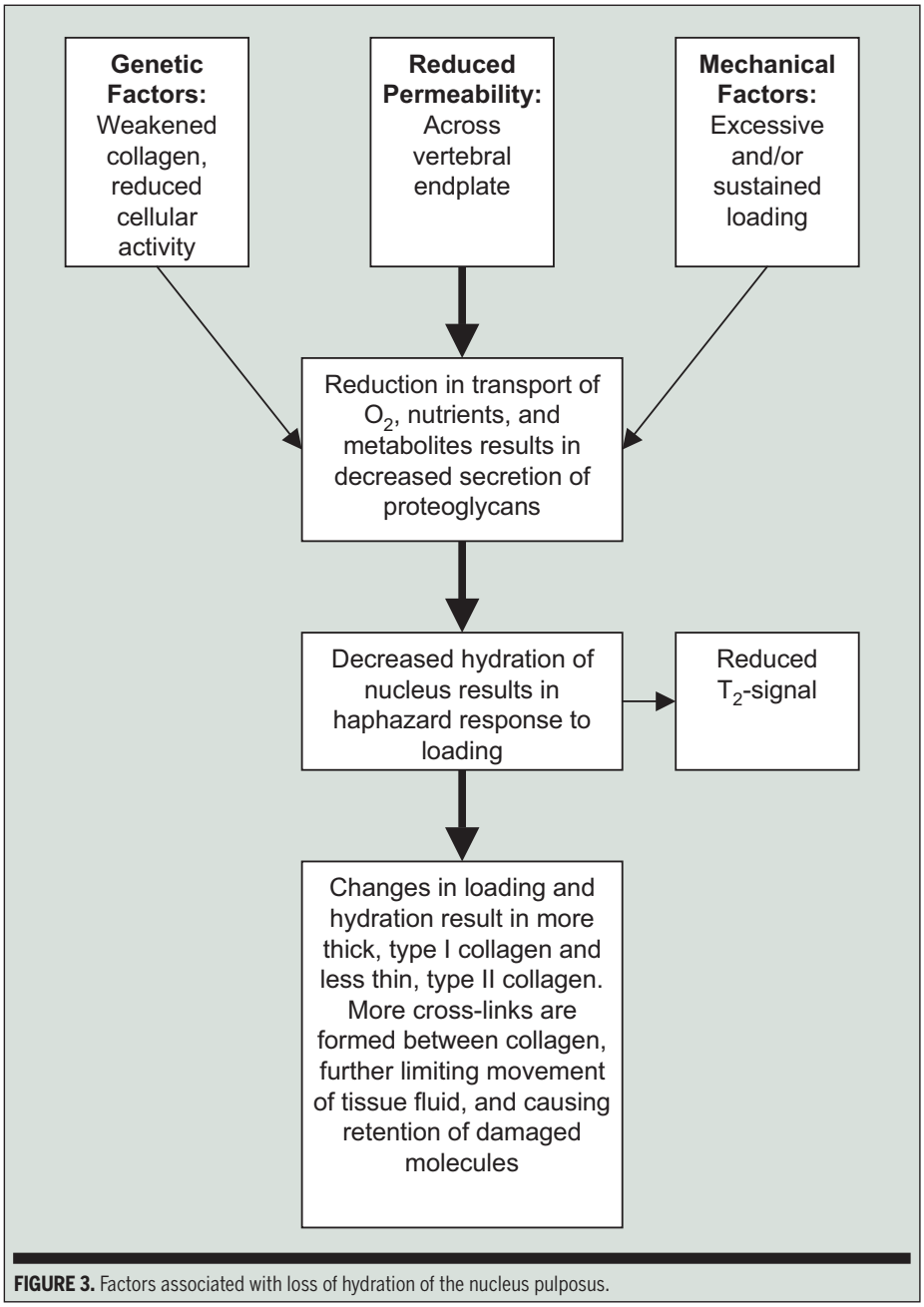

FIGURE 3. Factors associated with loss of hydration of the nucleus pulposus.

disturbance in the interplay between the nucleus and surrounding structures can lead to compromised function.[5]

Adams and Roughley[5] further illustrate this process as follows: a young, healthy IVD has high water content in the nucleus and in the inner annulus. This allows the IVD to behave like a "waterbed," with the outermost portion of the annulus acting as a restraining mechanism (the cover of the waterbed). In older discs, the water content decreases, forcing most of the annulus to resist compression directly, by acting as a solid restraint. In discs that have undergone structural disruption the nucleus is poorly supported by the annulus, resulting in a reduced or absent hydrostatic capacity of the nucleus. This causes the annular fibers to resist loads in a disorganized or irregular fashion. This can result in micromotion and loss of internal stability, resulting in further strain upon the disc structures (**ONLINE VIDEO**).

Etiologic Factors Related to Lumbar IVD Degeneration

Historically, it was believed that the strongest risks for the development of lumbar DD were environmental factors such as smoking, occupations involving heavy manual labor, and exposure to vibration.[43,82] Recent work by Batie and Videman[12,13,116] and others[6,105] has provided compelling evidence that, although environmental factors contribute to the incidence and progression of DD, the strongest predictors are the genetic factors which influence the size and shape of spinal structures, as well as the synthesis and breakdown of IVD structural components. By comparing lumbar MRI findings to lifestyle factors in a large sample of identical twins, Videman and Batie[116] reported a hereditability estimate of 74%. Interestingly, patients who were diagnosed with a herniated lumbar disc before age 21 were 4 to 5 times more likely to have a positive family history for this condition.[12] The hypothesis that genetics contribute substantially to the etiology of DD is also supported by the observation that DD has the highest prevalence in those people who also have evidence of osteoarthritis involving the extremities.[5,50] Another hypothesized etiology relates to programmed abnormalities of cell function, such as apoptosis (programmed death of cell).[58] For example, recent work has suggested that these unique cellular abnormalities are present not only in degenerative IVDs but in discs associated with scoliosis and spondylolisthesis.[58]

Exposure to smoking and a history of heavy physical loading have not been supported as meaningful etiologic factors of DD, and in the absence of trauma, competitive weight lifters actually have a lower than expected degree of degeneration.[12]

Age-Related Degenerative Changes in the IVD

It is generally agreed upon that while numerous events related to the aging process contribute to DD, a primary factor in this process is the reduction of the

IVD's nutritional capacity.[5,8,22,27,53,114] This occurs by several interrelated processes (**FIGURE 3**). Tissue fluid exchange between the IVD and the vessels in the vertebral bodies is reduced as endplate permeability and metabolic transport decrease,[84] which is associated with a reduction in the number of proteoglycan molecules within the matrix of the IVD.[53,81,104] This leads to a gradual loss of hydration that causes the nucleus to become smaller and decompressed, although it often retains its hydrostatic properties.[5] The relatively thin, type II collagen in the nucleus is replaced by the denser, type I collagen; concomitantly, there is increased cross-link formation between these collagen fibrils.[5,33] This creates a denser fibrous environment within the disc that is thought to further block tissue-fluid exchange.[33] The proteoglycans that remain within the disc may continue to perform their functional role; however, the barrier created by increased cross-links reduces the rate of turnover and repair of collagen and proteoglycans, altering IVD homeostasis and resulting in the retention of damaged macromolecules.[5] It is important to note that with these relatively benign, age-related changes there is not a substantial loss of disc height.[17,72] The typical T_2-weighted MRI finding is called a "dark disc," and is characterized by reduced brightness of the signal from the nuclear region, and/or the development of nuclear clefts (**FIGURE 4**).[14,51,79,92] It is of interest that the age-related changes that occur in the composition of the IVD are similar to those observed in articular cartilage and are not necessarily related to pain.[5,50]

Structural Disruption Associated With DD

Structural disruption of the IVD is manifested by a loss of the hydrostatic capacity of the nucleus that occurs when its surrounding connective tissues cannot provide adequate restraint.[5] This may occur following an injury to, or disruption of, the vertebral endplate and/or annulus.[8,65] Structural changes often initially occur in small, localized regions of the IVD.[58] Over time, tissue disruption can spread diffusely throughout the disc and lead to a reduction in stiffness and loss of fluid pressure, as well as various combinations of bulging, herniation, and decreased disc height.[5,9,62] These impairments lead to further alterations in local stress/strain relationships within the disc that can, in turn, cause adaptive changes in the anterior and posterior bony elements (**FIGURE 5**).[44,45,62,98]

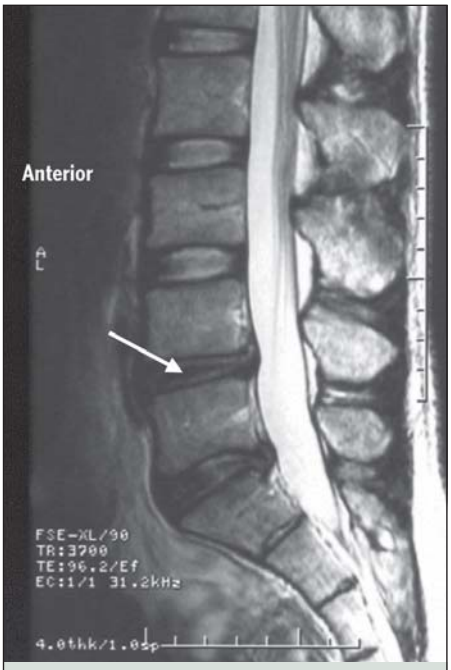

FIGURE 4. A midsagittal T_2-weighted MRI that illustrates early imaging signs of disc degeneration (reduced brightness of T_2-signal sometimes called a "dark disc") at L4-5 and L5-S1. Note the presence of nuclear "clefts" at the L4-5 intervertebral disc (arrow)

Endplate Disruption The vertebral endplate is believed to play a critical role in the transport of nutrients into the IVD and in the removal of waste products.[81,104,114] The endplate contains blood vessels in young individuals; however, these are typically absent by the second decade.[16,54] Following this, endplate permeability and disc metabolic transport across the endplate gradually decrease. Interestingly, at this time, the early signs of DD often begin to appear.

The endplate, previously described as the "weak link" in compression, is typically the failure point following axial trauma to the spine.[16,121] Disruptions of the endplate are increasingly being shown to have a strong relationship to DD,[25,78,80,81,98,121] presumably due to impairments of diffusion and a loss of "anchoring" of the annulus to the subchondral bone. Recent work[101] has suggested that, although they may be very similar in appearance, there are measurable differences in the diffusion capacity at the vertebral endplate between those IVDs with symptomatic degenerative disc and those with age-related changes. Rajasekaran et al[101] observed that alterations in the endplate produced distinct signs of disturbance in diffusion when measured by contrast-MRI. The authors suggested that aging and degeneration are 2 separate processes, as demonstrated by differences in diffusion rates.

Injuries to the endplate may often be visualized as having high signal intensity (when compared to bone marrow) on a T_2-weighted MRI (**FIGURE 6**). This MRI finding, known as a "Modic sign,"[59,78,81,121] has been postulated as a useful way to discriminate between painful and non-painful degenerative discs.[121] However, conflicting evidence exists regarding the specificity of this finding.[24-26,63-65,78] Endplate injuries are also frequently associated with bone marrow edema in the vertebral bodies and may cause a "Schmorl's node" to form in the adjacent vertebral body (**FIGURE 6**).[21,80]

In addition to its direct influence on the metabolic properties of the disc, injuries to the endplate can immediately decompress the nucleus, leading to a loss of its hydrostatic properties. Thus, endplate disruption can lead to impaired diffusion,[101] disruption in nutrient supply,[53] and/or cell death within the IVD, resulting from excessive tissue loading.[55,70,99]

Annular Disruption An early event in the structural failure of the IVD is the gradual disruption of the outermost and innermost layers of the annulus.[5,117] Annular disruption is very common, especially in the lower lumbar segments, and may be evident as early as age 10.[117] Three types of annular tears have been described.[5] These occur independently

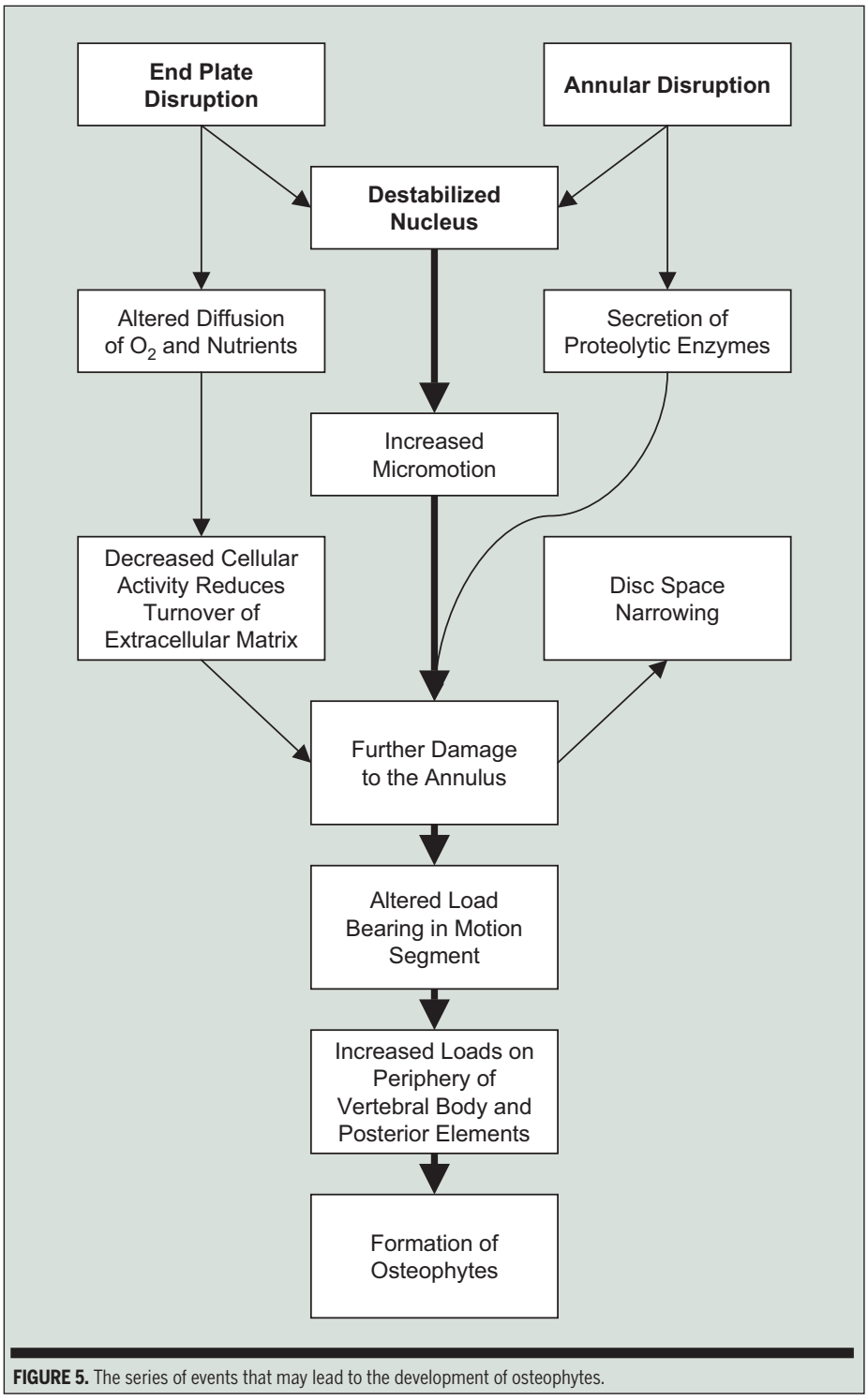

FIGURE 5. The series of events that may lead to the development of osteophytes.

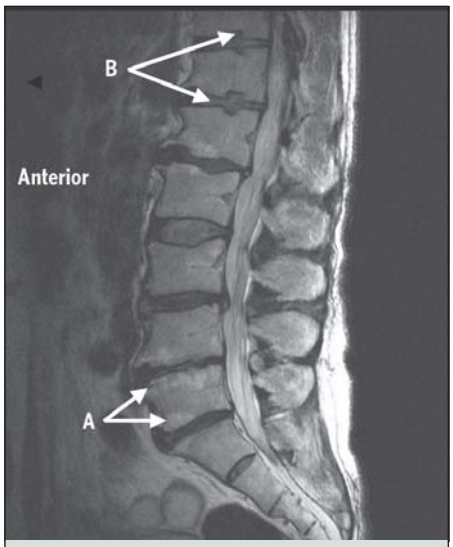

FIGURE 6. A midsagittal T_2-weighted MRI in a 64-year-old male that illustrates several common findings associated with advanced disc degeneration. The high (bright) signal in the superior and inferior margins of the L5 vertebral body (arrows marked A) is often called a "Modic Sign" and is thought to be bone marrow edema associated with damage to the superior and inferior vertebral endplates of the L5 vertebral body. Also note the narrowed disc space at L4-5 and L5-S1 and the anteriorly directed "disc osteophytes" caused by prolonged tension on the anterior longitudinal ligament from an anteriorly migrating L4-5 intervertebral disc. Schmorl's nodes are present at T11-T12 and T12-L1 (arrow B).

of age and one another, and may or may not be directly associated with symptom production.

Peripheral rim lesions primarily involve the outermost annulus and are likely to be in response to trauma.[86,87] Because these tears occur in a region that contains pain receptors, it is conceivable that they may act to generate symptoms.[35] High-intensity T_2 signals near the outer margins of the annulus have been described as representing hemorrhage or edema that may be associated with these tears.[68,91] The meaningfulness of this "high-intensity zone" (HIZ) (**FIGURE 7**) has been extensively investigated and, while it is highly correlated with pain production during discography,[68,91] it is also commonly observed in asymptomatic individuals.[26] Thus, this finding lacks specificity to identify pain-producing structures and should not be used in isolation to make clinical decisions.[26,68]

"Circumferential tears" represent splits between the layers of the annulus that may occur from repetitive compressive stress.

"Radial fissures" are disruptions in the annular regions that spread outward from the nucleus. These fissures are a primary structural abnormality associated with DD and can create pathways through which nuclear material can migrate, resulting in a destabilization of the nucleus and impairment of its hydrostatic capacity.[5,83,86]

Annular tears have a very limited ca-

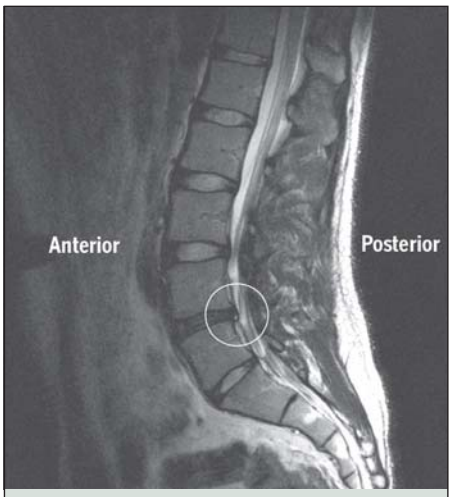

FIGURE 7. A midsagittal T_2-weighted MRI of a 34-year-old male with persistent low back pain, illustrating a high-intensity zone or HIZ (circle) in the posterior annulus of L4-5. This finding is believed to correspond to a tear in the peripheral annulus; however, there is conflicting evidence regarding its role in symptom-production.[26,68,90,91]

pacity to heal. Injuries to outer, vascularized portions of the annulus fibrosis have been shown to heal through inflammatory processes that result in poorly remodeled scars; however, because there is a very small concentration of cells in these tissues, it is difficult to break down the injured collagen and replace it with new collagen.[5,87] Larger lesions and those involving the avascular inner portions of the IVD are likely to be occupied by granulation tissue that does not restore normal tensile strength of the structures in this region.[87] In addition, abnormal stresses acting upon the IVD in response to annular tears may trigger the secretion of cytokines and proteases that may further inhibit healing.[5,8]

Interestingly, the body's attempt to heal annular tears may lead to further problems by increasing the area of the IVD that is innervated and by reducing the threshold to stimulation of pain-sensitive nerve fibers within the IVD. For example, inflammatory healing results in the growth of new blood vessels (neovascularity) that often penetrate deep into the annular region and are accompanied by pain-sensitive nerve fibers.[39,88,91] The growth of these nerves is further enhanced by inflammatory byproducts known as cytokines, which stimulate the expression of nerve growth factors.[1,9] In addition, a large array of chemical agents found in the healing IVD, such as substance P, interleukins, and tumor necrosis factor, may act to lower the threshold for triggering nocioception.[20,28,85,94,119,120] The result is that the somatosensory system may have an increased sensitivity to otherwise innocuous stimuli, such as occurs from standing or walking. This results in pain with these activities.[20,39,56,88] Although further research is needed, it is believed that variations in these biochemical responses to healing may contribute to the heterogeneity of various patients' rates of recovery from back injury.[9,20,21,110,111]

In addition to destabilizing the nucleus, injuries to the annulus and endplate can result in an impairment of diffusion of oxygen and nutrients into the disc, which accelerates the degenerative process.[5,27,53,61,84,104] For example, low oxygen tension in the center of the nucleus elevates anaerobic metabolism, resulting in a lower pH and a raised concentration of lactic acid.[113] This, in turn, can cause cells in the nucleus pulposus to become inactive. In addition, a chronic absence of glucose can result in cell death and lead to a build-up of metabolic waste products.[48,113,114] This results in a further reduction of pH that inhibits proteoglycan synthesis and leads to a reduction of hydration of the nucleus.[113] The resulting loss of internal stiffness in the disc increases micromotion during loading and may contribute to segmental instability.[20,42] This could lead to further tears in the annulus, especially radially directed ones, which, in turn, further disrupts diffusion and causes an increased secretion of proteolytic enzymes. Over time, the loss of water reduces the volume of the IVD, resulting in a reduction in disc height. Substantial loss of disc height can approximate vertebrae and slacken supporting fibrous tissues.[62,83]

Displacement of Nuclear Material Radial tears within the annulus often allow nuclear material to displace in the path of least resistance.[3,86] When enough nuclear material migrates to the periphery of the disc, this can result in a bulge,[57] sometimes called a "contained" herniation. Although MRI evidence of disc bulging can be dramatic, this finding is often not associated with symptoms.[15,23,57,97] In instances where nuclear material breaks free of its outer annular restraints and migrates into the lateral recess or vertebral foramen (a "noncontained" herniation), ipsilateral lower extremity pain and paraesthesia may be triggered.[15] This usually results from contact of extruded nuclear material with the dorsal root ganglia, resulting in the release of inflammatory byproducts and/or endoneurial edema resulting from reduced blood flow caused by pressure of the extruded material on the dorsal root ganglion.[20,28,29,56,122] This condition is most common in young and early middle-aged adults, and is rare in older adults or in severely degenerated discs that have limited fluid left in the nucleus.[5] Small and medium-sized herniations are often seen in asymptomatic people; however, large herniations (extrusions) and/or severe nerve compression are highly likely to be associated with ipsilateral, distal lower extremity pain.[15]

Extradiscal Changes Physiologic impairments resulting from degeneration of the lumbar IVD often have a direct or indirect influence upon adjacent structures.[44,45,62] A reduction in disc height of 1 to 3 mm can overload the facet joints and decrease the foraminal cross-section, due to inward bowing of the annulus and ligamentum flavum.[98] Repeated micromotion causes persistent stresses upon the longitudinal ligaments and outermost annulus, which stimulates osteoblastosis at their attachments, leading to osteophyte or "disc-osteophyte" formation (**FIGURE 6**).[62] This process is often associated with further loss of disc height and reduction in spinal range of motion that, in turn, further reduces the threshold for nociception during loading.[37,90] Load-bearing patterns can be severely altered (ie, with severe DD, 50% of weight-bearing loads are absorbed by the neural arch).[95] The

combination of posterior osteophytosis, severe disc narrowing, bulging of the annulus fibrosis, and ligamentum flavum can result in various degrees of compression of the neural elements within the lumbar spine that generate symptoms (ie, symptomatic spinal stenosis).[41,62]

CLINICAL RELEVANCE

A fundamental question asked by clinicians is, "To what degree does the presence of DD influence the way I treat my patient?" While it is highly likely that stimulation of pain-sensitive structures in the outermost annulus, subchondral bone adjacent to an injured vertebral endplate and/or adjacent tissues will trigger symptoms of low back pain or sciatica in certain patients under certain conditions, the current literature does not provide a valid system by which to use findings of DD to identify these patients; nor does it provide meaningful strategies to treat the specific pain-provoking tissues noninvasively. Considering this, classification systems for the physical therapy care of patients with low back pain have evolved based upon clusters of examination findings that predict the likely improvement in self-report measures in response to a given intervention (eg, manipulation, stabilization, specific exercises, and traction) rather than using pathology-based models to determine treatment.[40,64] So what, then, is the importance of knowing the degree of DD in your patient?

Physiologic Evidence to Assist in Treatment Decisions

Batie et al[12,13] have submitted that the effect of physical activity upon the degenerative IVD depends upon the time since the most recent episode of symptoms (recovery time), the stage of adaptation, and the overall magnitude of degeneration. For example, one could argue that for patients with mild, early-stage DD, where the disc height and hydrostatic nucleus are maintained, there would be no additional treatment precautions generated by the presence of DD. Interestingly, the use of graded weight training is supported in this population by evidence that suggests that, when performed properly, weight training does not result in adverse loads acting upon the disc[96] and, by the observation, that weight lifters do not have an elevated prevalence of DD.[12,13] No prospective studies that examined the effect of weight training on the progression of DD were located in the process of reviewing the literature for this clinical commentary.

For patients with later-stage DD, where the disc height is reduced and the hydrostatic nucleus is lost, physiologic evidence would suggest that care should be taken during loading progressions, especially in the presence of substantial damage to the endplate and/or annulus.[83] These injured structures are not likely to regain tensile strength,[5,86,87] thus exercises that stress vigorous or sustained loading at the end of the range of trunk motion must be avoided. Because of the alterations in disc diffusion and load-bearing patterns in degenerative IVDs,[31,36,61,83,84] symptoms may often occur several hours after the actual trauma to the degenerated disc. A patient may have a vigorous exercise session without noticeable symptoms but be unable to get out of bed the next morning. The use of lumbar stabilization exercises may improve a patient's ability to tolerate loading in degenerative discs and have a low potential for generating further injury. Studies have reported favorable outcomes in patients who have performed lumbar stabilization exercises,[10,11] and a clinical prediction rule has been proposed to identify those patients likely to improve.[52] The degree to which different degrees of DD influence these outcomes is, however, unknown.

The diurnal effects of disc fluid volume may also influence the response of degenerative discs to end-range loads, especially lumbar flexion. Snook et al[108,109] reported that patients with DD who avoided early-morning lumbar flexion had significantly less pain and disability than did those patients who performed early-morning lumbar flexibility exercises.

Other physiologic observations related to DD may influence patient management. For example, the intermittent compression loads absorbed by the spine during exercise or activities of daily living may be helpful; however, excessive or prolonged compression can lead to decreased activity or death of cells within the IVD.[37,70] Therefore, patients with DD must be strongly encouraged to avoid long exposure to compression (eg, prolonged sitting in flexed posture). Osteoarthritis involving the hips is often concomitant with DD.[50] Limitations in range of motion of 1 or both hips can have a profound influence upon loads acting upon the lumbar spine.

A critical but often overlooked factor is the powerful psychological effect of the diagnosis "degenerative disc disease."[38,92,118] Many patients may interpret this label as "deteriorating disc disease," and wrongfully believe that their spines are becoming weaker, leading to a life of severe, debilitating pain. This erroneous belief may be reinforced by some healthcare practitioners who try to motivate patients to undergo expensive and/or long-term courses of treatment. The powerful psychological impact of MRI evidence of DD can further enhance this process. Elevated fear-avoidance beliefs, disease conviction, and other adverse biobehavioral factors can potentially result.[38] Considering this, it is important that clinicians carefully communicate with patients to reassure them that DD is a normal aging process; while it certainly can be associated with episodes of pain, only in rare exceptions do these symptoms represent serious disease, and they should not, therefore, prevent one from performing reasonable activities.[118]

Future Directions in the Treatment of DD

Recent efforts are directed toward applying concepts of regenerative medicine to slow or reverse the process of DD by changing the internal environment of the IVD through the injection of various biomaterials, or implantation of load-

sharing devices.[66,67,76,106,119] Animal studies have shown favorable results, such as increased hydration following the injection of in vivo growth factor, autologous stem cells, or recumbent proteins into degenerative discs.[76,119] These findings are promising; however, it is unknown if they can be applied to humans and if these agents will be effective in the presence of severe structural damage to the disc (that is, there must be adequate annular restraints to maintain the hydrostatic nucleus).[5] Thus, while molecular therapies may prove to be revolutionary, they are clearly many years away from clinical use. Currently, systematic reviews suggest that only small, carefully selected subgroups of people with DD will have long-term benefit from surgical intervention.[46,47] Thus, nonoperative approaches may be the best option for the majority of patients with low back pain associated with DD. Interventions used by physical therapists, including manipulation,[32,74] the McKenzie approach,[73,77] and lumbar traction,[32,49,102] have been shown to have short-term effectiveness for pain reduction when used on specifically classified patients with low back pain[30,69,74,100,115] and have been purported, but not clearly demonstrated, to have a direct influence upon DD. Thus there exists a need for future study that addresses the specific physiologic effects of these interventions on the natural history of DD. This will provide valuable information regarding patient classification and treatment dosage and can assist in the development and refinement of cost-effective, safe treatment options for patients with DD.

SUMMARY

The development of lumbar DD is strongly linked to genetic factors, but its progression may be influenced by environmental factors. Loss of hydration of the nucleus is, in large part, the result of impairment of the diffusion of oxygen, water, nutrients, and metabolites. The hydrostatic properties of the nucleus can be maintained in the presence of degeneration as long as the annular components provide adequate support. Loss of annular support, however, is likely to lead to accelerated degeneration, loss of internal stability, and reactive bone formation. These impairments do not necessarily cause symptoms but may lower the threshold of the disc to sustain trauma that may influence pain-sensitive tissues in the outermost annulus, subchondral bone, or adjacent tissues. There are inadequate data to determine the influence of physical therapy interventions on the physiology of the IVD. The injection of biomaterials into degenerative IVDs may have promise; however, it is unlikely that these will be effective for severely degenerated IVDs. Future research should address mechanisms by which noninvasive, low-risk interventions, such as lumbar manipulation, traction, and exercise, influence the physiologic properties and natural history of DD. ◉

ACKNOWLEDGEMENTS: *The author would like to thank Richard Goodwin, PhD, and Claire Coyne for their kind assistance in the preparation of this manuscript.*

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