

Chapter 2

Intervertebral Disc Tissues

Michael A. Adams

Abstract Cartilagenous intervertebral discs separate adjacent vertebrae in the spine, allowing modest spinal movements, and distributing compressive load evenly on the vertebral bodies. A central fluid-like nucleus pulposus region is surrounded by a tough laminated annulus fibrosus. Because adult discs lack a blood or nerve supply, cell density is very low and tissue turnover is very slow. Consequently, discs have only a limited ability to heal following injury, and they exhibit a marked and progressive age-related deterioration in material properties. Changes in composition of old discs include fragmentation and loss of proteoglycans, loss of water (especially from the nucleus), and increasing cross-linking of collagens. Functionally, old disc tissues become dry, fibrous, and stiff. Pressure in the nucleus decreases, and stress concentrations grow in the annulus, which becomes more vulnerable to injury and herniation (“slipped disc”). Physical disruption allows nerves and blood vessels to grow into the tissue, which can become a source of chronic back pain. The aging annulus weakens, despite increased collagen cross-linking, because small defects accumulate in its lamellar structure, causing microscopic delamination. Progressive collapse of the annulus can trigger a “degenerative cascade” of events, including spinal osteoarthritis (as load-bearing is transferred to the neural arch), segmental instability, osteophytosis, and senile kyphosis.

2.1 Introduction

Intervertebral discs are pads of fibrocartilage which lie between the vertebrae of the spine. Age-related changes are particularly severe in intervertebral discs because they are the largest avascular structures in the human body, and have a low capacity for regeneration and repair. Aging impairs disc function. In addition, age-related

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changes in composition render the disc vulnerable to patterns of structural disruption, such as disc herniation (“slipped disc”), and these carry a high risk of causing degeneration, pain, and disability. For this reason, it is important to understand how the mechanical properties of disc tissues change with age.

The following section in this chapter gives an overview of intervertebral disc anatomy, function, aging, and degeneration. This is followed by a consideration of how whole discs function and fail when subjected to realistic mechanical loading, and how they are affected by aging. Novel techniques are described here for assessing the distribution of stresses and strains within discs, and for quantifying load-sharing between discs and adjacent structures. Section 2.4 then describes the tensile properties of the three tissues of an intervertebral disc: annulus fibrosus, nucleus pulposus, and cartilage endplate. The chapter ends with a summary of age-related changes in disc mechanical properties, and suggests some future research priorities.

2.2 Intervertebral Discs

2.2.1 *Anatomy*

Intervertebral discs have a soft deformable central region, the nucleus pulposus (Fig. 2.1), which is composed mostly of a proteoglycan gel held together loosely by a sparse network of type-II collagen fibrils. These fibrils have diameters in the region of 30–500 nm, and do not clump together to form gross fibers. However, they interact physically at certain nodal points to hold the tissue together (Fig. 2.2), and anchor it to adjacent tissues [109]. Proteoglycans are very large molecules with sugar subunits, which have a strong electrostatic attraction to water. Consequently, nucleus tissue swells greatly in water unless constrained by surrounding tissue and by applied mechanical loading. Loading causes the water content of the nucleus, which is approximately 80 % in a young adult [28], to vary diurnally by 20 %, being highest during night-time rest, and lowest following daytime activity [32].

The nucleus is surrounded by 15–25 concentric lamellae of the annulus fibrosus (Fig. 2.1c). Each lamella comprises parallel arrays of type I collagen fibers, running obliquely from one vertebra to the next [63], and surrounded by a proteoglycan gel. Chemical composition and structure change gradually from annulus to nucleus (Fig. 2.3), and the inner annulus is sometimes referred to as the “transition zone.” Annulus hydration reflects proteoglycan content, decreasing from around 80 % near the nucleus, to 60 % in the peripheral annulus [15, 28]. There is a corresponding increase in collagen content from inner to outer annulus, and the proportion of collagen that is type I increases from 0 to 100 % with increasing radial distance from the nucleus [90]. Collagen fibers in the outer annulus are anchored deep in the adjacent vertebral bodies, but in the inner annulus they appear to encircle the nucleus as they merge gradually into the cartilage endplate. Collagen fibers in

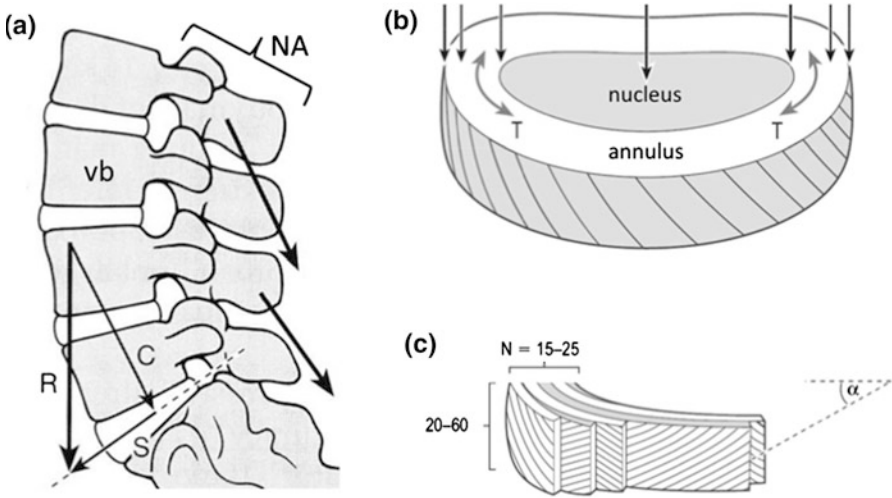


Fig. 2.1 **a** Lumbar spine showing intervertebral discs lying between vertebral bodies (vb). Forces on the spine (arrows) arise mostly from gravity, and from tension in muscles attached to the neural arches (NA) of each vertebra. Spinal compression (C) and shear (S) are defined as those components of the resultant force (R) that act perpendicular to, and parallel to the mid-plane of each disc. **b** Each disc has a soft nucleus pulposus surrounded by a tough annulus fibrosus. Hydrostatic pressure in the nucleus generates tension (T) in the annulus. **c** Details of annulus structure: each of 15–25 lamellae comprise 20–60 collagen fibers [63]. Images adapted from “The Biomechanics of Back Pain” [2], with permission of the publishers

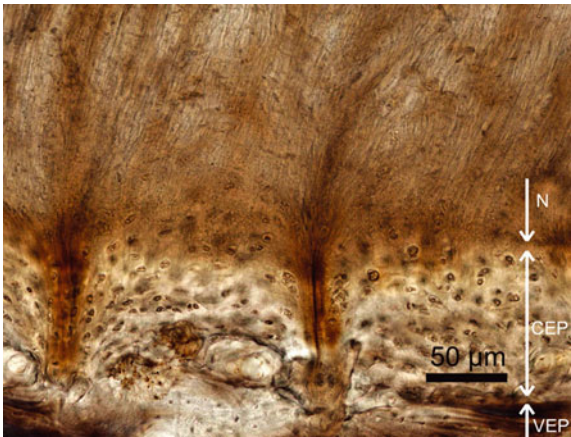


Fig. 2.2 Collagen fibrils in the (ovine) nucleus pulposus coalesce to form nodes which bind the nucleus (N) to the hyaline cartilage endplate (CEP) and the underlying vertebral (bony) endplate (VEP). Image obtained by Wade et al. using differential interference contrast microscopy [108], and reproduced with permission

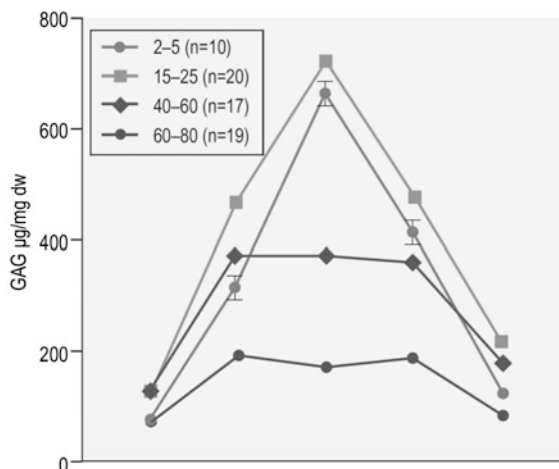


Fig. 2.3 Concentration of glycoaminoglycans (GAGs) within disc tissues varies with age, and with location from the outer anterior annulus (left edge of panel) through the nucleus to the outer posterior annulus (right edge of panel). GAGs are sugar components of proteoglycans. Data from Antoniou et al. [28]

the annulus have a planar zig-zag (“crimped”) structure, which enables them to be stretched more, as the crimps straighten out. Adjacent annulus lamellae are held together by discrete collagenous bridging structures (Fig. 2.4), which are orientated radially and wrap around individual collagen fibers, in a similar manner to ropes binding logs together in a raft. An intact annulus can swell only in the vertical (axial) direction, but radial swelling occurs also in small excised samples of tissue. Both annulus and nucleus contain a few percentage (by dry weight) of elastin, a fibrous protein, which can be stretched greatly without damage. The elastin network lies radially in the nucleus, and is concentrated between adjacent lamellae in the annulus [115]. It enhances the property of “elastic recoil”—the ability to recover shape following large deformations.

The third component of an intervertebral disc, the cartilage endplate, forms a thin layer, approximately 0.5 mm thick, between the disc and adjacent vertebral bodies (Fig. 2.2). It is composed of hyaline cartilage, and closely resembles the articular cartilage which covers the articulating surfaces of synovial joints. Hyaline cartilage has a similar chemical composition to the nucleus, but its high density of type II collagen fibrils forms a comprehensive three-dimensional network, which confers some rigidity, and (normally) prevents swelling [65]. The cartilage endplate is thickest adjacent to the nucleus and inner annulus, and is absent in the outer annulus. It is weakly bonded to the perforated cortical bone of the adjacent vertebral bodies.



Fig. 2.4 Image obtained using differential interference contrast microscopy showing annulus lamellae with collagen fibers approximately parallel to, or perpendicular to, the plane of the image. Several lamellae are bound together in the radial direction by a collagenous bridging structure (*). Reproduced from Schollum et al. [91] with permission

2.2.2 Mechanical Function

Deformable intervertebral discs allow small movements between adjacent vertebrae, so that the whole spine can bend and twist. Discs also distribute mechanical loading evenly on to the vertebral bodies, which form the main weight-bearing column of the spine. Remarkably, this capacity for load-distribution is little affected when the spine is bent, even when adjacent vertebral bodies are angled by 6° to each other [19] so that the annulus experiences considerable vertical strains [14, 17]. Human intervertebral discs are too stiff in compression [101] to act as efficient “shock absorbers” in the spine. However, some energy absorption can be achieved during locomotion by cyclic changes in spinal curvature, which lead to strain energy being absorbed by deformed intervertebral discs and ligaments, and by the tendons of those muscles which control spinal posture.

Disc mechanical functions reflect the materials properties of component tissues. The high water content of the nucleus (and inner annulus) enables it to exhibit a hydrostatic pressure when the disc is compressed [21, 70]. Lamellae of the annulus act primarily in tension to retain this fluid pressure, although the inner and middle annulus can also resist compressive loading directly [21, 64]. The high deformability of the annulus is achieved by several mechanisms: adjacent lamellae are only loosely bonded together; oblique collagen fibers can reorientate slightly when the annulus is stretched vertically [57]; and the crimp structure of Type I collagen fibers can “open up” to allow strains of 10 %, as in similar tissues such as tendon [92].

The cartilage endplate contributes to disc function by acting as a relatively dense filter, which reduces the rate at which water is expelled from the nucleus into the vertebral bodies when the disc is compressed. In this way, the cartilage endplate helps retain internal nucleus pressure under sustained loading. (Its role as a *biological* filter is also important [58], but beyond the scope of this chapter.)

The underlying bone endplate is part of the vertebra, but plays a vital role in disc mechanics. Under compressive loading, the virtually incompressible fluid nucleus presses on the bony endplate, causing it to bulge into the vertebral body by up to 1 mm [34]. This allows more volume for the nucleus, causing pressure within it to fall so that there is a relative shift in compressive load-bearing from nucleus to annulus. There is also a shift in load-bearing from the disc to adjacent structures, particularly the neural arches (Fig. 2.1a). In this way, the disc and vertebrae act in concert to distribute loading evenly, and minimize the risk of injury.

2.2.3 Forces Acting on the Discs of Living People

Intervertebral disc tissues are nonlinear and poroelastic. Nonlinearity implies that tissue stiffness, and hence load-sharing between adjacent tissues, varies with the magnitude of the applied load. Poroelasticity similarly implies that load-sharing varies with the *rate* of loading. Plainly, therefore, any investigation of disc mechanical failure requires that load magnitude and loading rates should reflect those encountered in life.

The “compressive” force acting on an intervertebral disc is the resultant force acting down the long axis of the spine, perpendicular to its mid-plane (Fig. 2.1a). Because the spine is curved, the direction of the compressive force varies with spinal level, as well as with posture. The spinal shear force acts perpendicular to the compressive force (Fig. 2.1a).

Approximately 50 % of body weight acts to compress the lumbar spine in upright postures. Much greater forces arise from tension in the paraspinal muscles, which stabilize the upright spine, and exert high moments to move it during activities such as manual handling (Fig. 2.5).

The spinal compressive force has been quantified in living people by inserting a needle-mounted pressure transducer into a disc nucleus, and then calibrating nucleus pressure against compressive loading in experiments on cadaveric spines

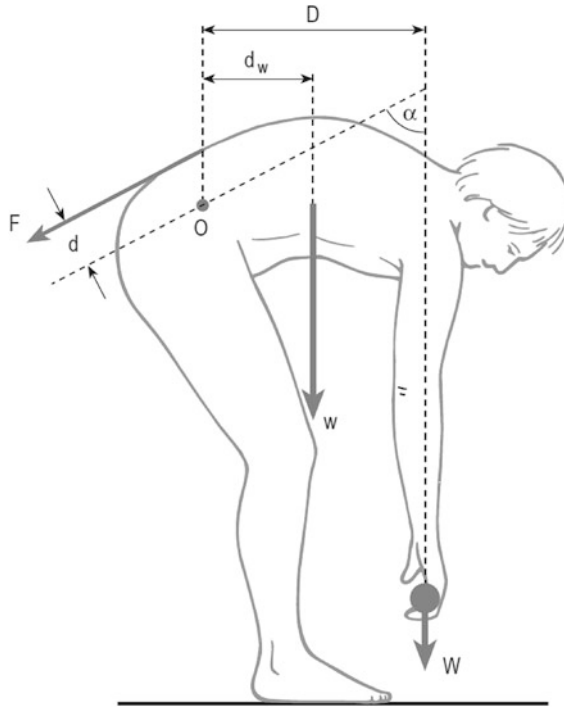


Fig. 2.5 Muscle forces acting on the spine can rise to high levels during manual handling. In order to lift the weight W , and upper body weight w , into the upright position, the man must generate a high tensile force F in his back muscles. These muscles act on a short lever arm (d) from the center of rotation (O) in the intervertebral discs, whereas the weight lifted (W) and upper body weight (w) both act on greater lever arms, D and d_w , respectively. Therefore, F is generally much larger than W , and exerts a high compressive force down the long axis of the spine. From “The Biomechanics of Back Pain” [2], with permission of the publishers

[71, 88]. Typical values are shown in Fig. 2.6. This invasive technique is not safe in vigorous activities; then an alternative strategy is to estimate spinal compression from the electrical activity of back and abdominal muscles. Electrical signals recorded from the skin surface overlying the back and abdominal muscles are calibrated against force generation during controlled static muscle contractions [41]. Such studies show that spinal compression typically reaches 3–5 kN during manual handling [43].

The greatest compressive forces on the spine usually arise when body weight is accelerated, for example during pilot ejection from an aeroplane, or when someone falls on their buttocks. These exceptional circumstances often cause the compressive tolerance of discs and vertebral bodies to be exceeded [113]. Even during everyday activities, rapid accelerations can increase spinal compression by more than 100 % compared to when the same movement is performed slowly [43].

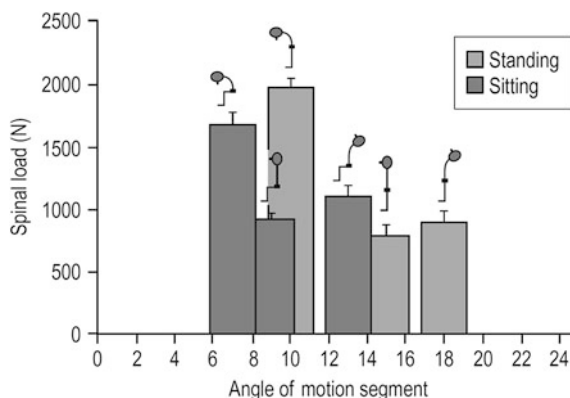


Fig. 2.6 Measurements of the compressive force acting on the lumbar spine during various standing and sitting postures [88]. A pressure transducer was inserted into the center of the L4-5 intervertebral disc in living volunteers, and pressures were then calibrated against force using cadaveric spines. Note how flexed postures increase spinal compression. Image from “The Biomechanics of Back Pain” [2], with permission of the publishers

Shear forces acting on lumbar intervertebral discs are not as great as might be imagined from Fig. 2.1a, because much of the anteriorly directed shear force on the *spine* is resisted by the apophyseal joints [99], especially after sustained loading causes stress-relaxation in the discs [39]. Back muscles also can resist anterior shear [85] so it is unlikely that shear injuries to discs are a common occurrence, unless the neural arch is damaged first. Similarly, axial torque (“torsion”) acting about the long axis of the spine is mostly resisted by the apophyseal joints, especially at lumbar levels [13], and little is known about peak torques acting directly on the intervertebral discs.

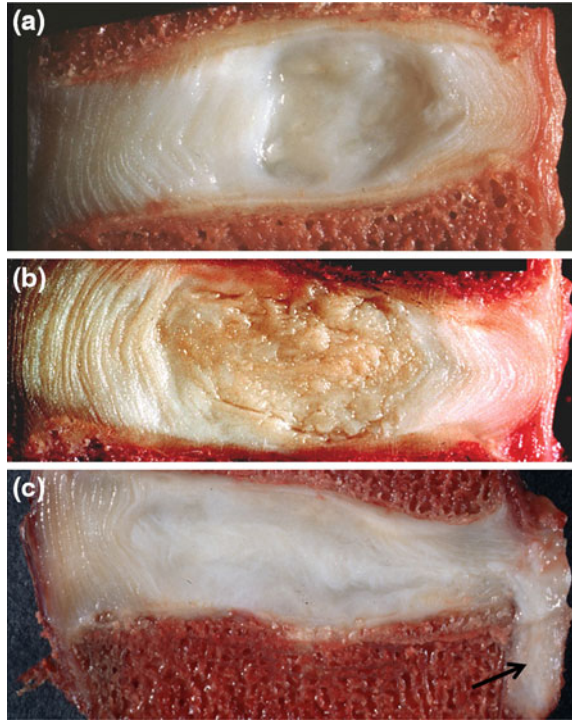
Spinal bending also can be resisted strongly by the neural arch, which appears to protect the disc in backward and lateral bending [19]. Forward bending (flexion), on the other hand, is resisted primarily by soft tissues, including the intervertebral discs and ligaments, and flexion is often cited as a contributing factors in spinal injuries, including disc herniation [93]. The forward bending moment acting on the lumbar spine rises to approximately 20 Nm during typical lifting tasks [4], with approximately 30 % of this being resisted by the disc [18]. The overall bending moment on the spine, and the disc’s share in resisting it, both increase in the early morning, when discs are swollen with water following a night’s rest [7].

2.2.4 Aging and Degeneration

Inevitable age-related changes appear first in the disc nucleus, and involve fragmentation and loss of proteoglycans (Fig. 2.3). This reduces the water content of the nucleus, and consequently its hydrostatic pressure [21]. More compressive

Fig. 2.7 Human lumbar intervertebral discs sectioned in the mid-sagittal plane (anterior on the *left*).

a Healthy disc from a young adult. **b** Healthy disc from a middle-aged adult, showing the biochemical signs of aging (see text). **c** Herniated disc from a young adult showing few signs of aging. A small quantity of nucleus pulposus (*arrow*) has herniated through the posterior annulus in response to severe mechanical loading [10]



load-bearing is thrown on to the annulus, as the disc behaves in the manner of an under-inflated car tyre. The other main constituent of the disc, collagen, also changes with age. The amount of Type I collagen increases, especially in the inner annulus [90], giving it a more fibrous texture (Fig. 2.7b). Collagen cross-links throughout the disc mature to nonreversible forms, and are augmented by adventitious cross-links involving sugars [95]. This “non-enzymatic glycation” causes the tissue to take on a brownish color (Fig. 2.7b). More importantly, excessively cross-linked cartilage becomes stiffer [110] and more easily injured [40]. Disc cell density decreases during growth, as metabolite transport difficulties increase, but then stabilizes around the age of 20 years [60]. However, an increasing number of cells lose the ability to replicate, and become less metabolically active [59].

Degeneration is difficult to separate from aging, because increasing age is a major risk factor for degeneration [37]. Nevertheless, the two processes should be distinguished as much as possible. There is a growing consensus that degeneration involves disruption of a disc’s structure, and that mechanical loading plays a major role in this [23]. Genetic inheritance also is important [30], as indeed it is in every physiological process, including growth and aging. Possibly, some gene variants lead to a weaker extracellular matrix [66, 81, 107]. Characteristic features of disc degeneration include: endplate fracture, circumferential fissures in the annulus (i.e., delamination), radial fissures in the annulus, disc herniation (Fig. 2.7c), internal

collapse of annulus lamellae, and biochemical changes, which are particularly advanced for their age [23]. Functionally, the nucleus becomes grossly decompressed [88] so that compressive load-bearing occurs mostly through the annulus. This in turn leads to annulus collapse, marginal osteophytes on the vertebral bodies, and reduction (or obliteration) of the disc space. There are many theories concerning disc degeneration, but the simplest (and most widely cited) is that structural damage permanently affects internal disc stresses, which impairs disc cell metabolism [9], while at the same time the structural disruption propagates by mechanical means [16, 49]. In effect, disc degeneration can be likened to “frustrated healing.”

2.2.5 Discogenic Pain and Disability

There are strong but variable associations between disc degeneration and back pain [37], and an even stronger one between disc herniation (arguably, a type of degeneration [6]) and radiating leg pain or sciatica. Physical disruption to the endplate or outer annulus allows focal swelling and loss of proteoglycans [102], which then stimulates the ingrowth of blood vessels and nerves [78]. Ingrowing nerves probably become sensitized by inflammation [76] or infection [27], both of which can be initiated by physical disruption. Sensitized nerves then signal severe and chronic pain because they are distorted by the gradients of compressive stress which become increasingly severe as disc degeneration proceeds (Sect. 2.3.4). Variable links between pathology and pain probably arise from the variable nature of pain-sensitization mechanisms.

2.3 Mechanical Properties of Whole Intervertebral Discs

2.3.1 Testing Large Cadaveric Spine Specimens

For reasons explained above, investigations of intervertebral disc function and failure should involve realistic (complex) loading and loading rates. This in turn requires hydraulic or electromechanical actuators to generate high forces quickly. Also, it is important to combine compressive and bending loads, possibly with shear and torsion also, because compressive loading is known to affect resistance to bending [55, 77]. A convenient technique is to offset the point of load application compared to the disc’s center of rotation (Fig. 2.8). This ensures that compression, bending and shear all increase at the same time, simulating what happens when a living person bends forwards. Other techniques include: using several hydraulic actuators to simulate forces arising from gravity and individual muscle groups [114]; using tensioned cables to simulate the resultant compression force arising from muscle activity while simultaneously applying a bending moment [77]; and using a robot arm to apply more than one component of loading at the same time [31].

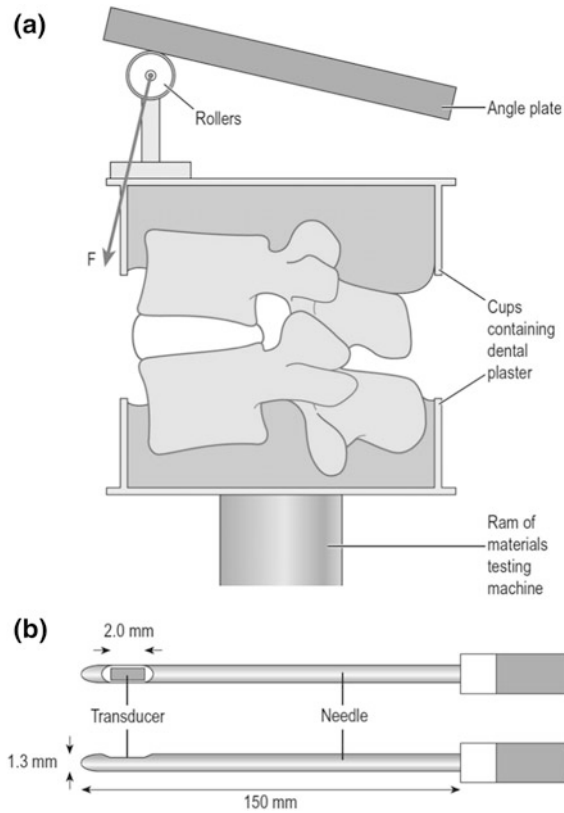


Fig. 2.8 a Method of applying realistic complex loading to a lumbar “motion segment” (basic repeating unit of the spine). The roller is positioned so that the applied force F , generated by a materials testing machine, applies a bending moment relative to the center of the intervertebral disc. The angle of the angle plate can be adjusted so that F also exerts any desired combination of compression and shear to the specimen, as defined in Fig. 2.1a. **b** Details of the pressure transducer that is pulled through loaded intervertebral discs in order to produce “stress profiles” as shown in Fig. 2.9. Images reproduced from “The Biomechanics of Back Pain” [2], with permission of the publishers

Another important consideration concerns the choice of specimen. “Motion segments” (Fig. 2.8a) represent the basic repeating unit of the spine and are economical on cadaveric material. However, they involve some disruption to the longitudinal ligaments, which contain fascicles spanning more than two vertebral levels. Longer spine specimens avoid this problem, but introduce the possibility of uncontrolled buckling in the middle “floating” vertebrae. Removing the neural arches makes it easier to isolate disc properties, but this can lead to unphysiological strains being applied to the disc, and interactions between discs and adjacent structures are then missed. A fuller account of testing methodology, including the influences of frozen storage and temperature, has been given elsewhere [2] [3]. Each

Table 2.1 Summary of experimental data concerning the strength of lumbar spine motion segments (MS), and of intervertebral discs with their adjacent vertebral bodies (Disc)

Loading	Site of failure	Strength (STD)	Comments
MS—compression	Endplate	10.2 (1.7) kN	Male specimens
MS—shear	Neural arch	2 kN?	Uncertain
MS—forwards bending	Posterior ligaments	73 (18) Nm	Compressive preload
MS—backwards bending	Neural arch	26–45 Nm	Disc damage possible
MS—torsion	Neural arch	25–88 Nm	
Disc—compression	(See above for MS)		Neutral/erect postures
Disc—shear	Annulus?	0.5 kN?	
Disc—flexion	Posterior annulus	33 (13) Nm	Compressive preload
Disc—torsion	Annulus	10–31 Nm	Delamination occurs

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technique has its strengths, drawbacks and areas of applicability. None is ideal, and all can yield valuable information.

2.3.2 Resistance to Bending and Compression

Mechanical properties of cadaveric lumbar motion segments tested in bending and compression are summarized in Table 2.1. The last four lines of this table refer to specimens in which the neural arches have been removed, and so indicate properties of isolated, whole intervertebral discs.

There is little systematic data showing how whole disc properties change with age. Perhaps the most instructive concern the strength in forward bending of isolated disc-vertebral body specimens, tested to failure in combined bending and compression [12]. Regression analysis showed that, between 20 and 70 years of age, strength decreased by 43 %, from 40 to 24 Nm. Many other experiments have shown that the spine becomes weaker, stiffer and less mobile with increasing age (summarized in: [2]) although some of these changes are attributable to altered properties of spinal ligaments and bones. There is some evidence that spine specimens become more mobile following early degenerative changes in the discs, perhaps indicating a transient “segmental instability” [116], but then stiffen greatly when degeneration is severe [47], possibly because of the growth of vertebral osteophytes [25].

2.3.3 Viscoelastic Properties of Whole Intervertebral Discs

Sustained compressive loading causes discs to “creep” at a decreasing rate before reaching an equilibrium height after several hours. The most important underlying mechanism is water loss, especially from the nucleus and inner annulus [67].

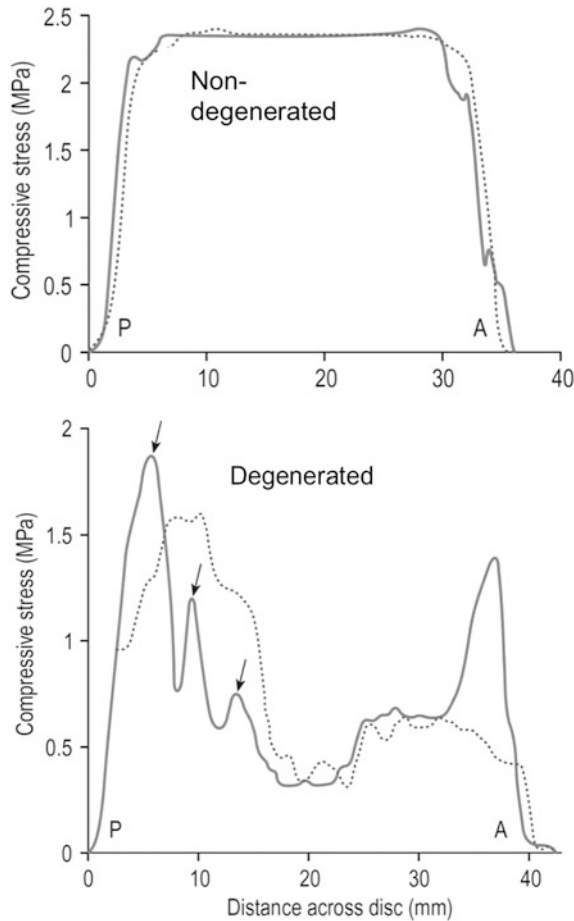


Fig. 2.9 “Stress profiles” indicate how the intensity of loading (measured with the pressure transducer shown in Fig. 2.8b) varies across the mid-sagittal diameter of cadaveric lumbar intervertebral discs. In this experiment, discs were compressed by 2 kN. Posterior and anterior margins of the disc are denoted P and A. The *solid line* shows vertically acting stresses, measured with the transducer membrane pointing upwards, and the *broken line* indicates horizontally acting stresses. In a healthy young disc (upper diagram) the measured stresses vary little with location or direction, indicating fluid-like properties. This region includes most of the anatomical annulus as well as the nucleus. In a degenerated disc (lower diagram) the nucleus pressure is low, and high stress concentrations and gradients appear in the annulus (*arrows*). Images from “The Biomechanics of Back Pain” [2], with permission of the publishers

However, some height loss is attributable to adjacent tissues [82, 106] and to structural changes within the discs, which bulge radially as load-bearing is transferred increasingly from nucleus to annulus [20, 35]. This latter process probably explains the “slow” creep response described by some mathematical models [73]. If disc compressive creep is analyzed using a simple spring-dashpot model, it

becomes apparent that increasing age is associated with decreasing viscous modulus (E_1) and decreasing viscosity (η). These changes probably indicate, respectively, increased resistance to compression by the neural arch following water expulsion from the disc, and decreasing resistance to fluid expulsion from old proteoglycan-depleted disc matrix [84]. Because compressive creep loading reduces the height of the intervertebral disc, it generates some slack in the posterior intervertebral ligaments, and thereby increases the range of spinal flexion movement [5].

Sustained bending also produces viscoelastic effects in intervertebral discs and ligaments. Rapid flexion movements increase the peak bending moment resisted by 10–15 % compared to slow movements, and 5 min of sustained flexion reduce it by 42 % [5]. These changes are largely attributable to fluid flow, and are probably greater in ligaments than discs because fluid flow path lengths are greater in the disc.

2.3.4 Distributions of Stress and Strain Within Intervertebral Discs

The “stress profilometry technique was introduced to investigate how compressive stresses vary within and between disc tissues. A pressure transducer, side-mounted in a hollow catheter (Fig. 2.8b), is pulled across the diameter of a loaded intervertebral disc so that graphs can be plotted of “stress” against distance [21]. The resulting “stress profiles” (Fig. 2.9) form a bridge between the mechanical properties of a whole disc (considered in this section), and those of its component tissues (considered in the next). Because the transducer is side-mounted (Fig. 2.8b), the catheter can be rotated about its long axis to measure “stresses” acting in different directions. The transducer is calibrated in a fluid, and so is suitable for measuring the extent of the fluid region in the middle of the disc (the “functional nucleus”). More controversially, it appears to measure axial compressive stress even within the annulus fibrosus of old and degenerated discs. This assertion is based on an analysis of transducer output when inserted into small cubes of annulus, which were subjected to known compressive stresses [38, 68]. The fact that transducer output is approximately equal to applied stress suggests that restoring forces generated within the cube of annulus, which would act to prevent the tissue from deforming into the recess of the catheter (Fig. 2.8b), have little effect [38]. This is equivalent to saying that stress coupling between disc tissue and transducer membrane was almost perfect, in the inner and middle annulus as well as in the nucleus. In the peripheral annulus, transducer output was poorly related to compressive stress, presumably because this fibrous tissue is more solid than fluid, and acts predominantly in tension [69]. The quasi-fluid behavior of certain disc tissues under certain circumstances will be considered again in Sect. 2.4.5.

Typical stress profiles obtained across the anteroposterior diameter of loaded human discs are shown in Fig. 2.9. With increasing age, the hydrostatic pressure in

Table 2.2 Grade of disc degeneration influences the distribution of an applied compressive force between the anterior and posterior halves of the disc, and the neural arch

Condition of disc	Distribution (%) of applied compressive force		
	Anterior disc	Posterior disc	Neural arch
Normal/mature	32 (27)	49 (25)	19 (8)
Mild degeneration	21 (20)	41 (20)	38 (18)
Severe degeneration	10 (8)	12 (8)	78 (9)

Data represent average (STD) values for cadaveric motion segments tested in a simulated upright posture [22]. Note how severe disc degeneration concentrates compressive loading on the neural arch

the nucleus and inner annulus decreases, and localized stress concentrations arise in the middle annulus, especially posterior to the nucleus [21]. These effects are exaggerated in degenerated discs (Fig. 2.9b) as disc narrowing causes compressive load to be rerouted through the neural arches, reducing overall loading of the disc [83]. However, stress *gradients* (the rate of change of compressive stress with distance) increase inexorably with increasing disc degeneration [103], explaining the progressive annulus delamination and collapse which characterizes advanced disc degeneration.

Intradiscal strains have been studied as well as stresses. Internal strains can be measured from distortions of a grid of radiopaque wires implanted into a cadaveric disc, which is then compressed [105]. Age-related disc degeneration significantly increases radial displacements of annulus lamellae, as well as circumferential tensile strains. Similar results were reported using a noninvasive magnetic resonance imaging (MRI) technique to quantify internal deformations of annulus lamellae under load [74].

2.3.5 Load Sharing Between Discs and Adjacent Tissues

In an extension of the above-mentioned technique, stress profiles were effectively integrated over area in order to quantify the total compressive force acting on different regions of the disc [83]. Furthermore, the compressive force acting on the whole disc could be calculated and compared with the applied compressive force in order to quantify how much of the applied compression was resisted by the “posterior column” of neural arches (which acts in parallel with the “anterior column” of discs and vertebral bodies). Results depended on spinal level and posture, but there was clear evidence that, with increasing age, compressive load-bearing decreases markedly in the anterior regions of the disc and vertebral body, and moves increasingly from the anterior to the posterior column (Table 2.2). This major age-related change in disc function can be attributed to the effects of disc narrowing on adjacent structures, and it explains why disc degeneration often precedes degenerative changes in the apophyseal joints [36]. Stress-shielding of the

anterior vertebral body in elderly spines also explains why it becomes so weak, and vulnerable to the anterior “wedge” fractures, which are common in elderly women, especially those with senile kyphosis [22].

Forward bending moments applied to the osteoligamentous lumbar spine are resisted mostly by the posterior intervertebral ligaments, with the disc contributing an average 29 % of resistance in full flexion [18]. In backward bending, the disc resists an average 33 % of the applied bending moment [8], and in axial rotation, it resists 37 % of an applied axial torque [13], with the balance coming (in both cases) from the neural arch.

2.3.6 Mechanisms of Disc Mechanical Failure

Many experiments on cadaveric spines have shown that compressive overload always leads to fracture of the vertebral body endplate, before any damage can be detected in the disc. Compressive strength depends very much on bone mineral density (BMD) [33], and so decreases with age, typically from 10 kN in the lumbar spine of young men [53] to 2 kN in the thoracic spine of elderly women [62]. Endplate fracture creates more space for the disc nucleus, and so causes an immediate decompression of the adjacent disc, often by 50 % or more. This effect, which is greater in the narrow upper lumbar and thoracic discs [44], can then lead to internal disruption and degenerative changes in the affected disc [10].

Overloading the lumbar spine in shear, torsion or backward bending leads to compaction of the neural arches, with damage probably occurring in the apophyseal joints before the disc is affected [2]. Stress-shielding of the disc by the neural arch increases with age, as disc height decreases and as osteophyte growth progresses in the apophyseal joints.

Excessive anterior bending of the lumbar spine sprains the posterior intervertebral ligaments at a flexion angle of 10–20°, and an average bending moment of 50 Nm [18]. At this “physiological limit,” the disc resists an average 13 Nm without apparent harm. The strength in anterior bending of an isolated disc is 33 Nm on average, with failure usually occurring near the disc-bone junction in the outer posterior annulus [12].

Intervertebral discs can be made to prolapse (or “herniate”) if compression and bending are combined, as they often are during manual handling (Fig. 2.5). This combined loading stretches and thins the posterior annulus at the same time as increasing nucleus pressure: the result is often a posterior herniation of nucleus pulposus through a radial fissure in the most-stretched region of annulus [10, 14] as shown in Fig. 2.7c. Lower lumbar discs are most likely to fail in this manner, especially if the nucleus has a high water content, and the annulus is showing the first signs of age-related weakening. These conditions ensure that disc herniation occurs most easily in spines aged 40–50 years [14]. Similar disc lesions can be created by less severe but cyclic loading in bending and compression [16].

2.4 Tensile Properties of Small Disc Samples

2.4.1 Problems Inherent in Testing Small Specimens Excised from a Large Structure

Intervertebral discs have an irregular three-dimensional structure made up of three tissues, one of which (the annulus fibrosus) is markedly anisotropic and inhomogeneous (Fig. 2.1c). Tensile properties therefore vary greatly between tissues, and with orientation and location within each tissue.

A further problem is that removing a small sample of tissue disrupts its collagen network, with disruption being in inverse proportion to sample size (Fig. 2.10). Essentially, annulus fibrosus behaves like a “chopped fibre-composite” material [11, 72], with stiffness being proportional to the average length of the collagen fibers, which reinforce the softer matrix by a mechanism of shear stress transfer with surrounding softer matrix. (This is generally how collagen fibers behave, and the word “collagen” actually means “glue maker”.) The approximately linear relationship between the size and stiffness of small annulus samples (Fig. 2.10) makes it possible to extrapolate to full disc size, and suggests that stiffness and strength are reduced by more than 50 % when small specimens (typically $2 \times 2 \times 15$ mm) are removed from an intact annulus.

Despite these complications, several experiments (reviewed below) have paid enough attention to standardize the location, orientation and size of tissue samples

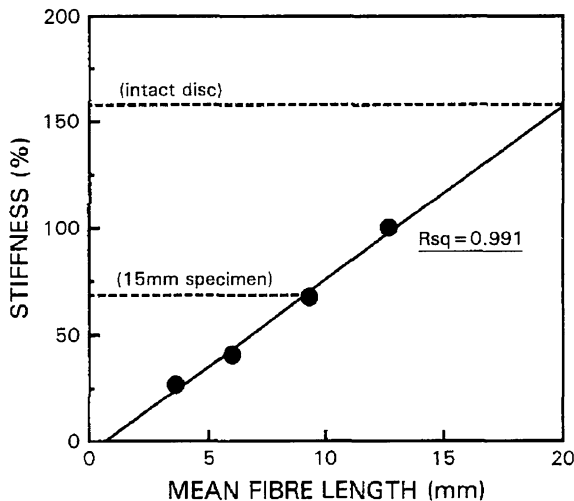


Fig. 2.10 Experimental data showing how the tensile stiffness of small samples of human annulus fibrosus depends on the mean length of collagen fibers within the sample. Mean fiber length was varied by making successive cuts through the specimen, in the direction of the applied tension but at an angle to most collagen fibers [11]

that age-related changes in materials properties can be ascertained. Most experiments have considered only the annulus, although some preliminary data is available for nucleus pulposus and cartilage endplate.

2.4.2 *Methods of Tensile Testing*

A cutting tool incorporating parallel razor blades is generally used to remove parallel-sided samples of disc with consistent geometry (Fig. 2.11). Frozen (or partially thawed) tissue is easier to cut, although there is some evidence that freeze-thaw cycles can alter annulus properties slightly, especially if freezing is performed slowly at -20°C rather than at -70° [48]. A second tool can be used to obtain dumbbell-shaped specimens (Fig. 2.11) that are likely to fail in the narrow section, well away from the clamps where the tissue is subjected to abnormal complex stresses.

To secure disc specimens in the clamps of the testing machine, cyanoacrylate (“superglue”) can be used to glue both ends of the disc specimen to the smooth face of sand- or emery- paper, which is folded over the specimen (Fig. 2.11). Compression clamps can then hold the rough face of the paper without being tightened to such an extent that the ends of the specimen carries the risk of being damaged.

A more elaborate technique involves bi-axial testing of small annulus specimens [50, 54, 75] in order to minimize the artifactual Poisson effect that can occur in small isolated specimens.

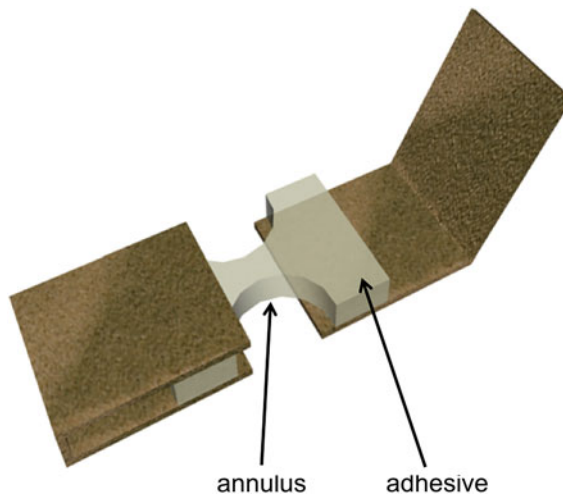


Fig. 2.11 Convenient method of gripping small dumbbell-shaped specimens of annulus for tensile testing. Emery paper is folded over each end of the specimen, and an adhesive (“super-glue”) is used to bond the wet specimen to the smooth face of the paper. The rough outer surfaces of the paper can then be gripped securely in the clamps of a testing machine

2.4.3 Tensile Properties of the Annulus Fibrosus

A major early experiment on small specimens from one or two lamellae showed them to be stiffest and strongest when tested parallel to the collagen fibers, and weakest at right angles to the collagen fibers [48]. Later experiments on larger specimens showed them to be softer and weaker when stretched vertically (in the axial direction) in a manner which characterizes spinal bending, compared to when they are stretched circumferentially, in a manner that characterizes spinal compression. After correcting for the weakening effect of excising small samples from an intact annulus (see above), it was predicted that in situ strength of the annulus in the vertical direction is 3.9 MPa for the anterior annulus and 8.6 MPa for the posterior [11]. Annulus specimens are softest and weakest when stretched radially, perpendicular to the lamellae [46, 72]. Failure of multi-lamella specimens usually involves delamination combined with individual collagen fiber bundles being pulled out from the proteoglycan-rich matrix (Fig. 2.12).

Stiffness and strength increase from inner to outer annulus (Table 2.3), as collagen content (and the proportion of Type I collagen) increases [45, 98]. Tensile properties are also reduced in the posterior and posterolateral annulus compared to the anterior [45, 48].

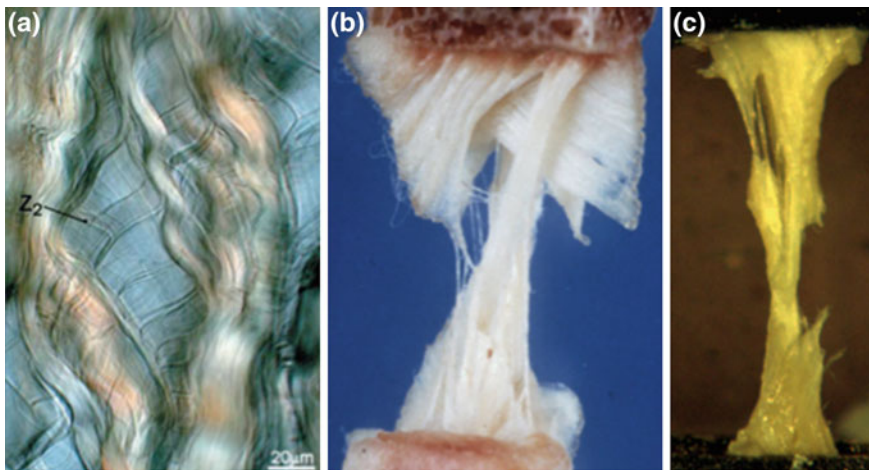


Fig. 2.12 Images of small annulus specimens under tension reveal details of collagen organization, and failure mechanisms. **a** This undamaged bovine specimen was pulled laterally to reveal the crimped and interweaving nature of the collagen network. Reproduced from Pezowicz et al. [80] with permission. **b** This multi-lamellar human specimen was pulled to failure in the vertical direction. Note the alternating collagen orientation in successive lamellae. Failure has occurred by delamination, and by some collagen fibers (coated in proteoglycans) being pulled from the surrounding matrix. **c** Failure of this small sample is similar to that shown in (b). Reproduced from “The Biomechanics of Back Pain” [2], with permission of the publishers

Table 2.3 Representative tensile properties of annulus fibrosus, derived from uniaxial tension tests on small annulus samples from human lumbar discs aged 48–91 years [98]. Values refer to the mean (STD)

	Inner annulus	Middle annulus	Outer annulus
Failure stress (MPa)	2.0 (1.5)	4.1 (2.3)	7.4 (4.3)
Failure strain (%)	64 (36)	44 (15)	40 (11)
Normalized stiffness	1.20 (1.11)	2.77 (1.62)	5.67 (3.38)
Failure energy (N mm)	15.5 (13.7)	21.6 (15.4)	33.2 (23.9)

The structural parameters “Normalized stiffness” and “Failure energy” can be compared between regions because all specimens were of similar size

Time-dependent properties have received some attention. Annulus specimens exhibit stress-relaxation, and residual elongation, and are stiffer when stretched quickly [48]. Fatigue failure can occur in less than 10,000 cycles if the tensile force exceeds 45 % of the UTS [49].

2.4.4 Age-Related Changes in Annulus Tensile Properties

Annulus stiffness tends to increase with age and degeneration, consistent with the known increases in collagen content and cross-linking, although the effect is small and variable [1, 48]. Theoretical analyses of experimental data concerning human annulus suggest that age-related degenerative changes increase modulus by up to 200 %, with the greatest increases seen in the “toe-region” (i.e., at low strains), and when the annulus is stretched radially [72, 75].

Annulus *strength*, however, appears to decrease with age. When tested in the circumferential direction, small samples of annulus show variable weakening with increasing age and degeneration [1, 45, 94]. Samples of outer annulus show the greatest changes: a 40 % reduction in strength with increasing grade of disc degeneration [94] and a 66 % reduction in strength (in male discs only) between the ages of 48–91 years [98]. Greater strengthening and subsequent weakening of the outer annulus may be attributable to its greater cell density [52], which makes it more responsive to adaptive remodeling. The gender influence could be explained by a greater tendency for men to undertake hard physical labor. Annulus changes (in men) mirror reductions in compressive strength in the adjacent vertebral bodies [98]. Tensile strength in the radial direction also decreases with advancing age-related disc degeneration, typically by 30 % [46].

It may appear paradoxical that aging annulus should become weaker, even though it becomes stiffer. The most likely explanation is that weakening is due primarily to macroscopic defects accumulating in the tissue, especially circumferential splits between the annulus lamellae [51].

2.4.5 Tensile Properties of the Nucleus Pulposus

The hydrostatic properties of the nucleus have caused its tensile properties to be virtually ignored, but this is unfortunate because it does have a collagen network, and any displacement of nucleus into (or through) the annulus is likely to be of clinical significance (Fig. 2.7c). Stress gradients have been reported in the nucleus of cervical intervertebral discs [100], using the technique described in Sect. 2.3.4, even though horizontal and vertical “stresses” are equal at each location. This behavior has been likened to a “tethered fluid,” in which the material is sufficiently soft to equalize stress over short distances, even though its reinforcing fibers become entangled and resist strongly under high tensile strains. Phase-contrast microscopy can demonstrate strain-related changes in the organization of Type II collagen fibrils in the nucleus, and how they firmly bind the nucleus to the endplate (Fig. 2.2) and to the surrounding annulus [109] when strains are high.

Preliminary experiments in our own laboratory have confirmed that small samples of nucleus, tested as described in Sect. 2.4.2, provide negligible resistance to tension at strains of up to 30 %, but then resist increasingly. Depending on location and orientation, ultimate tensile strain averaged 63 % (range 26–110 %) and ultimate tensile stress averaged 0.26 MPa (range 0.08–0.64 MPa) (Gholkar, Adams: unpublished data). No age-related data for the nucleus are available. It would be expected that the increasing concentration of collagen in the aging nucleus (and the increasing proportion of type I collagen), would cause old nucleus to become stiffer, stronger and less deformable, although collagen degradation in degenerative conditions could exert an opposite influence [29].

2.4.6 Tensile Properties of the Cartilage Endplate

This topic also has been ignored, perhaps because it is assumed that endplate properties are similar to those of articular cartilage, which has been more extensively investigated [104]. In a normal intervertebral disc under load, the cartilage endplate is pressed against the underlying bone by the fluid pressure in the nucleus pulposus (see Figs. 2.2 and 2.9). Nucleus pressure can fall to zero in severely degenerated discs [62], and negative pressures (a “vacuum phenomenon”) have occasionally been reported when the spine is put into traction, or when it is bent backwards in supine postures [111]. Under these circumstances, it would be possible for the cartilage to be pulled off the subchondral bone. This failure mechanism has been demonstrated on cadaveric specimens with the hyaline cartilage “peeling off” in a straight line, close to its junction with bone [49, 58].

Although poorly characterized, this failure mechanism could be important in disc herniation. “Erosive” lesions of the bony endplate (consistent with cartilage being stripped from it) are common in the lower lumbar spine [112], where most disc herniations occur. Furthermore, fragments of endplate cartilage have been

observed in many disc herniations [86], where they are associated with persistent sciatica [94]. The relative stability and persistence of endplate cartilage fragments can be attributed to their dense network of collagen Type II fibrils, which usually prevent fragments of hyaline cartilage from swelling [65]. In contrast, fragments of annulus fibrosus or nucleus pulposus swell greatly, and increasing pore size then facilitates proteoglycan loss [42]. A fragment of endplate cartilage in a herniation is therefore likely to persist as a relatively hard fragment, one that does not permit ingrowth of blood vessels (which are repelled by proteoglycans [56]), and so does not spontaneously “resorb” in the body. The possibility that such cartilage fragments arise from the endplate is important for another reason: the underlying perforated cortical bone endplate is freely permeable to large molecules and cells [87], so focal loss of the cartilage layer could allow bacteria to enter the disc from the vertebral body, and inflammatory mediators to enter the vertebral body from the disc. In this way, focal loss of cartilage from the endplate could explain persistent sciatica, disc infections, and inflammatory events (“Modic changes”) in the bony endplate [26].

2.5 Summary and Conclusions

2.5.1 *Discogenic Pain and Disability*

Pain and disability arise from degeneration of intervertebral discs, rather than from “normal” aging. Degeneration involves structural defects in the annulus or endplate, which have a permanent and harmful influence on disc cell metabolism, and which allow reinnervation and revascularization. Age does not lead inevitably to disc degeneration, but is a strong risk factor for it, because age weakens the disc’s extracellular matrix, while reducing the population of viable cells that might counter accumulating “fatigue” damage. Other major risk factors for disc degeneration are an unfavorable genetic inheritance, and environmental influences such as severe physical loading. This is the context in which age-related changes in the mechanical properties of disc tissues contribute to the etiology of discogenic pain and disability.

2.5.2 *Age-Related Changes in Disc Mechanical Properties*

Age-related changes in the mechanical properties of a whole intervertebral disc are fundamentally due to changes in the composition, and hence materials properties of the three component disc tissues. The most important changes in composition are: fragmentation and loss of proteoglycans, and increasing cross-linking of collagen. Proteoglycan loss reduces tissue water content, and prevents the disc from distributing load evenly. This effect is greatest in the nucleus, and loss of nucleus

hydration and pressure causes an overall shift in compressive load-bearing from nucleus to annulus. Increased collagen cross-linking causes disc tissues to become stiffer and more brittle with age. This effect is greatest in the annulus, where it reinforces the shift in load-bearing from nucleus to annulus. The aging annulus weakens, despite increased stiffening, because small defects accumulate in the lamellar structure, including microscopic delamination. Changes in disc composition cause old intervertebral discs to bulge slightly, and to weaken, but mechanical function is little affected. Age-related changes in composition are particularly severe in intervertebral discs because they are the largest avascular structures in the body. Cell density is correspondingly low, and insufficient to turnover and repair an extensive matrix. Consequently, it takes years to replace damaged proteoglycans and collagen in human discs [96, 97].

Disc degeneration, which occurs if the disc's structure becomes disrupted, is characterized by progressive loss of disc height, and exaggerated radial bulging [23]. These changes often lead, in turn, to the growth of vertebral body osteophytes, and apophyseal joint osteoarthritis. The spine becomes shorter, stiffer, and less mobile.

2.5.3 Suggestions for Future Work

Most of the changes seen in aging intervertebral discs are essentially benign: they have little effect on disc function, and are not in themselves painful. In the opinion of the author, intervertebral disc research should aim to prevent the structural disruption, which causes some aging discs to degenerate. Ergonomic interventions could reduce accidents, and physical exercises could increase disc strength and flexibility. Another aim should be to assist healing in those regions of the disc (such as the outer annulus and endplate), which have a sufficiently high cell density to repair matrix defects. This might involve physical or pharmacological therapies similar to those used to treat injured tendon or bone [24]. A third aim, perhaps the most important, is to tackle directly the causes of discogenic pain. This could involve preventing blood vessels, nerves, and bacteria from growing into a disrupted disc, perhaps by using “fillers” such as fibrin glue in the annulus [89], or bone cement near the endplate [61]. An alternative strategy would be to disable ingrowing nerves [79] or block their sensitization by interfering with inflammatory pathways.

From a materials science standpoint, future research on intervertebral discs should aim to describe more fully the manner in which collagen fibers reinforce their matrix. This could lead to interventions to improve tissue mechanical properties, for example by increasing collagen cross-linking [89, 103] in such a manner that strength is increased without any loss of toughness.

2.6 Conclusions

With increasing age, intervertebral disc tissues become less hydrated, more fibrous, stiffer, and marginally weaker. Underlying mechanisms are loss of proteoglycans, increased collagen cross-linking, and microstructural damage. These tissue changes are essentially benign, but they increase the risk of major structural damage, which can then lead on to degeneration and pain. Future disc research should concentrate on blocking mechanisms of structural disruption and pain, rather than trying to reverse the aging process.

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