Basic science of spinal degeneration

Alex Torrie

Michael A Adams

Abstract

This updated review summarizes advances in our understanding of spinal pathology and pain. Degenerative changes start in the intervertebral discs, often in the second decade, and can be distinguished from normal ageing by the presence of physical disruption, typically in the form of annulus fissures, prolapse, or endplate fracture. Physical disruption is mechanical, but frustrated attempts by a small cell population to heal a large avascular matrix give rise to the biological features of disc degeneration. Genetic inheritance and ageing can predispose to disruption and degeneration. Discogenic pain probably arises from the peripheral annulus and endplate, as ingrowing nerves are sensitized by chemicals diffusing from activated disc and blood cells. A degenerated disc loses internal pressure and bulges like a flat tyre. This reduces the disc's resistance to bending, but the resulting 'segmental instability' can be reversed by osteophytes growing around the margins of the vertebral body. Annulus collapse in severe disc degeneration transfers compressive load-bearing to the neural arch, leading to facet joint osteoarthritis, and possibly to degenerative scoliosis. The anterior vertebral body becomes stress-shielded, causing focal bone loss (exacerbated by systemic osteoporosis) which increases the risk of anterior wedge deformities, and kyphosis. Recent interventions to reduce pain include disc prostheses with no moving parts, antibiotics to counter disc infection, and injection therapies to block pain pathways.

Keywords Back pain; biomechanics; degeneration; intervertebral disc; osteoporosis

Introduction

The adult spine is a common source of pain, deformity and disability. Research has traditionally concentrated on disc degeneration in the middle-aged, and vertebral osteoporosis in the elderly. However, there is increasing awareness that degenerative changes in discs and vertebrae are interdependent, both mechanically and biologically.

The present article reviews the pathophysiology of spinal degeneration from a mechanistic basic-sciences viewpoint. A brief introduction to functional anatomy of the spine is followed by a description of intervertebral disc degeneration, and how it relates to ageing and to disc prolapse. Changes in elderly vertebral bodies are explained in terms of altered load-sharing combined with underlying age-related bone loss. In fact, most degenerative changes in the ageing spine are interconnected, and can be viewed as a 'degenerative cascade'. Final topics include 'sagittal balance', and recent advances in treating patients with spinal degeneration and pain.

Alex Torrie *MB ChB MRCS (Eng) is Spinal Registrar and Research Assistant at the Centre for Comparative and Clinical Anatomy, University of Bristol, UK. Conflicts of interest: none declared.*

Michael A Adams *BSc PhD is Professor of Biomechanics, and Senior Research Fellow in the Centre for Comparative and Clinical Anatomy, University of Bristol, UK. Conflicts of interest: none declared.*

Functional anatomy of intervertebral discs and vertebral bodies

Intervertebral discs are pads of fibrocartilage between the vertebral bodies (Figure 1). They distribute stress (force per unit area) evenly on the bones, while allowing limited movements between them. The neural arches of vertebrae surround and protect the spinal cord, with their bony prominences acting like levers so that attached muscles and ligaments can create (or limit) spinal movements. The apophyseal joints are plane synovial joints which stabilize the spine and protect the discs from high shear and torsion.

The central region of a disc, the nucleus pulposus, is a soft hydrated gel which acts like a fluid to distribute compressive load evenly on the vertebral bodies. It is restrained by the surrounding anulus fibrosus, which comprises concentric lamellae of collagen fibres, arranged in alternating directions (Figure 1). Adjacent lamellae are loosely bonded to each other by collagen and elastin fibres, and peripheral lamellae are firmly embedded into the adjacent vertebrae. Adult discs are normally avascular and aneural.

Vertebral bodies are short cylinders of trabecular bone with a thin shell of cortical bone. Vertebral cortex lying adjacent to the disc is referred to as a vertebral endplate. Endplates contain many small perforations in their central regions which allow metabolites to pass between bone marrow and the disc nucleus. A thin layer of hyaline cartilage is weakly bonded to the disc side of the endplate: it acts as a biological filter and helps maintain fluid pressure in the nucleus. Both the hyaline cartilage and cortical bone layers are normally included in the term 'endplate'.

Intervertebral disc degeneration and prolapse

With increasing age, the disc nucleus loses some of the proteoglycan molecules that bind water in to the tissue,[1] causing a drop in nucleus hydration and pressure.[2] The disc bulges radially with a 'middle-aged spread'. Increasing cross-linking of the disc's collagen causes it to become stiffer and more fibrous, and to develop a yellow/brown discolouration (Figure 2a and b). Disc cell density declines throughout growth, presumably as a result of increasing metabolite transport difficulties in the avascular tissue. After skeletal maturity, cell density remains constant, although more of the cells become senescent.

Intervertebral disc degeneration is rather different: it is characterized by structural damage to the disc matrix,[3] combined with increased activity of matrix-degrading enzymes.[1] This can be interpreted as attempted repair (Figure 3), which is largely frustrated by the low cell density, and by repeated damage. Typically, structural damage takes the form of fissures in the annulus (sometimes allowing nucleus herniation), and focal defects in the endplate. Both can be created by mechanical loading in cadaveric experiments.[2] Degenerated discs have a decompressed nucleus, and high compressive stress concentrations in the annulus.[4] These changes cause the annulus to bulge radially outwards like a flat tyre, or to collapse inwards, and the disc loses height (Figure 2c). Usually there is some ingrowth of nerves and blood vessels.[5]

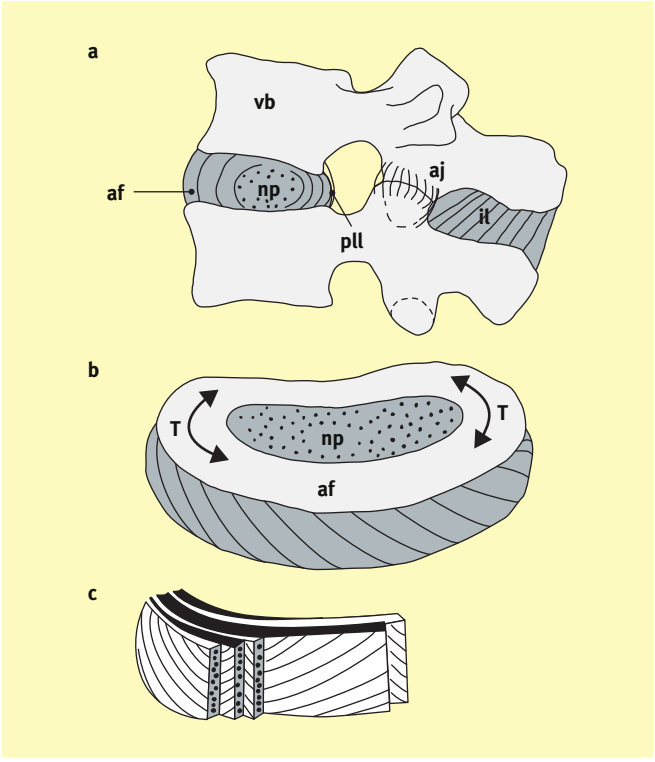

Figure 1 (**a**) The basic functional unit of the spine is the 'motion segment' made up of two vertebrae, an intervertebral disc and ligaments. The disc lies between adjacent vertebral bodies (vb) and comprises a soft nucleus pulposus (np) surrounded by the annulus fibrosus (af). The disc is stabilized by a pair of small apophyseal joints (aj), and flexion is limited by the interspinous ligament (il). (**b**) Compression of the spine generates a fluid pressure in the nucleus, and tensile 'hoop' stresses (T) in the annulus. (**c**) Layers (lamellae) of the annulus have collagen fibres passing obliquely between the vertebral bodies, with the fibre direction alternating between successive lamellae.

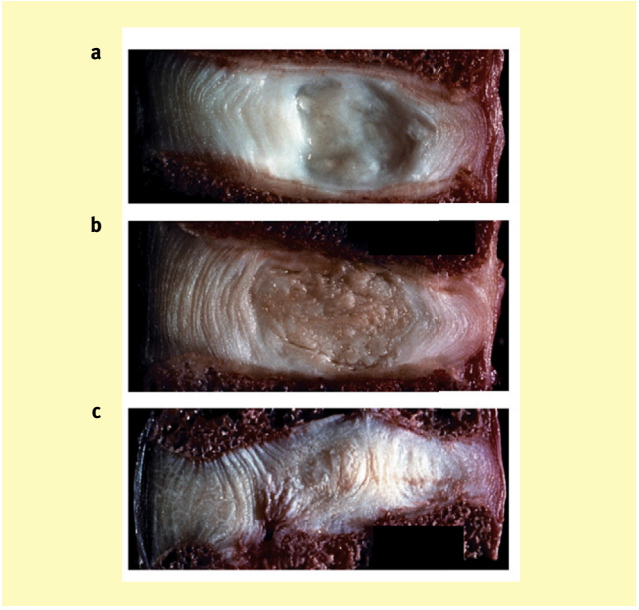

Figure 2 Mid-sagittal sections through human intervertebral discs, anterior on the left. (**a**) Non-degenerated, young adult. (**b**) Non-degenerated, middle-aged. (**c**) Severely degenerated, young adult. Stress concentrations in the annulus increase with age, and become large with degeneration. (Reproduced from *The Biomechanics of Back Pain* 3rd Ed. by Adams et al.,[2] with permission of the publishers.)

The causes of disc degeneration are controversial,[3] but the major underlying risk factors are increasing age, and an unfavourable genetic inheritance.[6] Age makes the matrix more brittle and less able to distribute load evenly, and an unfavourable inheritance appears to involve genes that affect matrix strength and metabolism. Evidently, some discs are so weakened by inheritance and ageing that the matrix can become physically disrupted during the activities of daily living. The complementary roles of genes and environment are illustrated by the fact that genetic susceptibility to disc degeneration is least in the lower lumbar spine,[6] where mechanical loading is highest.

Discogenic pain is associated with the physical disruption that accompanies degeneration rather than with the biochemical changes of ageing. Hence, recent population studies show a strong dose—response relationship between back pain and disc degeneration revealed by MRI.[7] Discogenic pain appears to depend on 'pain-sensitization' phenomena in which chemical messengers diffuse from disturbed nucleus cells[8] or from blood cells, and alter the firing threshold of nerves growing inwards from the outer anulus or endplate.

Disc prolapse (or herniation) involves nucleus material moving radially outwards through an anulus fissure to such an extent that the disc periphery is affected. Herniation usually affects L4-5 and L5-S1 discs, and is strongly associated with spinal bending movements.[9] Herniation can be viewed as a distinct 'phenoptype' of disc degeneration[10] or as a separate condition. The finding that histological changes in herniated discs are distinct from those found in discs that have degenerated without herniating suggests that a disc need not be degenerated before it herniates.[11] Recent studies show that disc herniation can involve the annulus tearing part of the cartilage endplate from its subchondral bone[12] leading to persistent sciatica.[13] Loss of the cartilage 'filter' may explain why endplate inflammation ('Modic

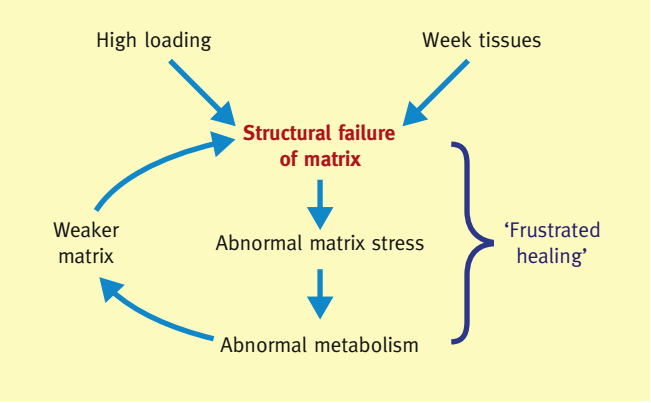

Figure 3 Schematic suggesting how structural failure of the extracellular matrix is a crucial step in disc degeneration. Failure can be caused by high loading of normal tissue, or normal loading of tissue that has been weakened by age and/or unfavourable genes. Damaged matrix resists mechanical loading unevenly, and abnormal matrix stresses interfere with disc cell metabolism, resulting in weakening and further structural damage. This 'vicious circle' can be characterized as 'frustrated healing' because of the inability of the relatively low population of disc cells to fully repair their extensive matrix. (Adapted from Adams et al.[2])