Robert J. Moore

The vertebral end-plate: what do we know?

Received: 18 November 1999
Accepted: 10 December 1999

R. J. Moore
Division of Tissue Pathology, Institute of
Medical and Veterinary Science,
Department of Pathology,
University of Adelaide, Australia

R. J. Moore (✉)
PO Box 14 Rundle Mall,
Adelaide SA 5000, Australia
e-mail: rob.moore@imvs.sa.gov.au,
Tel.: +61-8-82223219,
Fax: +61-8-82223204

Abstract The vertebral end-plate is critical for maintaining the health of the intervertebral disc. This paper reviews the literature that relates to end-plate structure and development and describes how disc integrity is affected by changes associated with pathology and aging. A range of studies, including biomechanical, biochemical, surgical and histological is discussed to illustrate the important role of the end-plate in spinal function.

Key words Spine · Intervertebral disc · End-plate · Disc degeneration

Intervertebral discs are discrete components of the axial spine that occupy approximately one-third of its length and separate the vertebral bodies. The obvious functions of the discs are to confer flexibility to the spine and to facilitate a range of complex movements. In addition, they also transmit mechanical loads through dissipation of energy, although this function tends to be over-interpreted by some authors who describe them as “shock absorbers”. With the exception of the sacrum and the first cervical level, all 23 discs in the human spine have a similar general structure. The *annulus fibrosus* forms a firm, but flexible, outer layer that surrounds the central compressible *nucleus pulposus*. The *end-plates* that lie at the cranial and caudal interface of the disc on one side, and the vertebral body on the other, are the other major structural component of the disc, albeit lesser recognised than the other two. Rather than merely being transitional tissue that happens to lie between the disc and the vertebral body, the end-plates of a healthy disc prevent the highly hydrated nucleus from bulging into the adjacent vertebral bone, while simultaneously absorbing hydrostatic pressure that results from mechanical loading of the spine [7].

Whether the end-plates should be considered as part of the disc or the vertebral body has been discussed at length

since the time of Schmorl earlier this century [41]. It is not critical to understanding the role of the end-plate, but it is important to appreciate that the end-plate comprises an osseous component as well as a hyaline cartilage component. In most discussions, however, the end-plates are considered to be the thin layer of hyaline cartilage that lies between the bone of the vertebral body and the soft tissue of the disc.

In simple terms, the cartilaginous component of the end-plates consists of a gel of hydrated proteoglycan molecules that is reinforced by a network of collagen fibrils [25]. Following skeletal maturity, the population of cells that is arranged homogeneously within this network consists mainly of chondrocytes, but without the distinct strata seen in articular cartilage. In most other respects the structure is similar to that of articular cartilage, and while the end-plate cartilage is not connected directly to the bone of the vertebral bodies, it does have direct connections with the disc through the lamellae of the inner (medial) annulus fibrosus [20]. In the adult disc the end-plates typically are less than 1 mm thick, and although this varies considerably across the width of any disc, there is a tendency for the end-plate to be thinnest in the central region adjacent to the nucleus pulposus [37].

The biochemical composition of the end-plate in normal, aging and degenerate conditions has been well documented [2, 3, 34] and appears to be much more like articular cartilage than epiphyseal cartilage [37]. There are several species of collagen found in disc tissue, but type X, in particular, has received considerable attention, particularly in relation to the end-plates, because it is a marker of hypertrophic chondrocytes and is thought to be involved in cartilage calcification [1]. Type X collagen is found mainly in the central region of the cartilage end-plate, and histological staining patterns indicate that it increases with advancing age [23]. There is a view that degenerative changes result from abnormal calcification in the region of the end-plate [1, 35].

The biochemistry of the end-plate is critical in maintaining the integrity of the disc. Proteoglycans, in particular, appear to regulate the transport of essential solutes into and out of the disc, to the extent that loss of proteoglycans from the end-plate ultimately leads to loss of proteoglycans from the nucleus pulposus [38]. Disturbances of the biochemical composition of the end-plate during growth have further been implicated in the development of scoliosis [33, 36].

The end-plates are recognisable as discrete entities at an early stage in the development of the axial skeleton and remain as cartilaginous plates during the subsequent ossification of the vertebrae [42]. In this earliest period, tiny blood vessels penetrating the end-plates provide nutrition, not only for the cartilage itself, but also for the developing disc that eventually becomes enveloped by the annulus fibrosus and the vertebral body. These blood vessels persist only until skeletal maturity, at which time the discs become, for the most part, avascular. It is a curious feature of mammalian discs that they have evolved with such a sparse blood supply. In fact, the largest discs in the adult human lumbar spine can be up to 20 mm from the nearest blood vessels, making them the largest avascular structures in the body. Apart from a sparse blood supply in the outer layers of the annulus, mature discs are almost totally reliant on diffusion of solutes across the cartilage end-plates for nutrition.

The complex mechanisms of disc nutrition and metabolism have been studied extensively. In early qualitative studies of disc metabolism, the central zone of the end-plate and the entire annulus fibrosus were shown to be permeable to diffusion of small dye molecules, while the lateral regions of the end-plate near the vertebral rim were relatively impermeable [28]. The permeability was attributed to the presence of small vascular buds in the medullary space immediately beneath the end-plate. This work was confirmed by subsequent quantitative studies using human autopsy specimens, which showed that the central part of the disc in the vicinity of the nucleus pulposus had relatively more vascular marrow contacts than the periphery [25].

Using elegant vascular injection techniques, Crock and Yoshizawa [14] demonstrated a network of arteries and

veins that concentrated within the central one-third of the vertebral bodies and, in turn, on the corresponding end-plates. The function of this vascular network, specifically in relation to the nutrition and metabolism of the constituent cell population of the disc matrix was investigated subsequently using *in vivo* and *in vitro* experiments [46]. These studies showed that diffusion of dissolved molecules from the subchondral vessels is the principal mechanism for small solute transport into the discs. There are, however, other aspects that affect the movement of solutes through the disc matrix. For example, although solutes theoretically are free to diffuse into the disc by either the annulus or the end-plate route, their actual movement is directly dependent on the size of the molecule as well as its ionic charge [45, 46]. By virtue of the high proteoglycan concentration, the normal disc has an overall negative charge, which means that small, uncharged solutes such as glucose and oxygen diffuse relatively freely into the disc matrix. Negatively charged molecules such as sulphate and chloride ions cross the end-plate relatively easily, but have difficulty passing through the nucleus pulposus. Cations, such as sodium and calcium, exchange freely with the nucleus. Larger uncharged solutes, such as immunoglobulins and macromolecules including enzymes, tend to be totally excluded from the normal disc simply due to their size. Clearly there are two important factors influencing diffusion of solutes into the disc: the proportion of vascular contacts at the end-plate, and the steric properties of the solutes involved.

The permeability of the disc itself varies across the different regions of the disc from almost free transfer through the annulus to virtually nil through the rim at the point where the annular fibres are embedded in the end-plate. The central end-plate route is also freely permeable, although not to the same extent as the annulus. The relative importance of these two routes was established further by Ogata and Whiteside [31] using a hydrogen washout technique, and by Holm et al. [18] using microscopic examination following fluorescent dye injections. Crock and Goldwasser [13] used radiological and histological techniques to characterise the vascular terminations at the vertebral end-plate of greyhounds and reinforced the increasingly widely held belief that the central region of the end-plate was vital for the metabolic processes of the disc matrix that is otherwise avascular.

By early adulthood the cartilage of the end-plate has undergone a substantial degree of mineralisation [5, 30]. This tissue, in turn, undergoes resorption and replacement with bone, a process that most likely impedes diffusion and nutrient flow between the vertebral marrow and the disc. In addition, the blood vessels within the end-plate become obliterated by calcification, further limiting the exchange of nutrients. Roberts et al. [35] attributed modifications in solute flow between the disc and the vertebral marrow to increased remodelling in the region of the end-plate and subchondral bone.

Despite compelling evidence to the contrary, the mature end-plate in some species does appear to have the capacity to become vascularised in normal conditions [32] and also following trauma to the discs [26]. This suggests that vascular channels can proliferate after maturity under unusual physiological circumstances, presumably to maintain adequate nutrition of the disc. Carreon et al. [9, 10] however, hold the opposite view, although it should be noted that the tissue in these cases was actually outside of its usual environment and not functioning normally. The creation of blood vessels in the end-plate is facilitated by the activation of enzymes such as matrix metalloproteinases (MMP) and their tissue inhibitors, which are latent under normal conditions [12, 15, 22]. MMP-3 (stromelysin) in particular has been detected in high concentrations in degenerate discs [21].

Blood flow in the region of the end-plate is not entirely passive, as there are muscarinic receptors present that can influence disc nutrition under altered physiologic conditions [49]. A recent immunohistochemical study has identified nerve fibres growing into the end-plate and subchondral bone along with blood vessels in degenerative discs [8], suggesting that repair tissue in damaged discs is implicated as a source of pain. This study requires validation by other workers, but opens up a new area for clinical and laboratory investigation of back pain.

As indicated earlier, the end-plate is also important in the mechanical function of the spine. Just as loading influences the overall shape of the disc, there is a specific effect on the end-plate, with axial compression in particular resulting in deformation of the cartilage end-plate and underlying trabecular bone [6]. A young healthy cartilage end-plate may regain its shape after moderate loading, but it is possible that sufficiently high compressive loads, especially when applied repeatedly, may result in irreversible damage. In fact, it appears that the integrity of the end-plate and the subchondral bone, rather than the degree of disc degeneration, determines the extent of damage during compression [19]. Further, the radiographic appearance of the end-plates in this particular study was similar to those of patients with osteoporosis. In osteoporotic patients, the end-plate becomes increasingly concave with age in association with loss of bone density, particularly in subchondral trabeculae [43, 44].

The end-plate appears to be susceptible to mechanical failure as this is a weak link in the structure of the disc. Using finite element modelling to analyse the potential for different scenarios to induce disc degeneration, Natarajan et al. [29] showed that mechanical failure of the vertebral motion segment always began with separation of the end-plate from the subjacent bone. This theoretical approach agreed precisely with the earlier microscopic observations of Vernon-Roberts [47], who found that clefts and tears appearing from middle age originated in the vicinity of the end-plate and ran parallel to it. This was also confirmed by the autopsy study of Tanaka et al. [40] in which it was

postulated that the end-plate first becomes separated from the vertebral body and is subsequently herniated from the disc along with anchoring fibres of the annulus fibrosus. There is further evidence of this scenario in a recent histological study [27] in which almost half of 120 herniated disc specimens contained at least some end-plate fragments. Fracture of the posterior vertebral end-plate is common in adolescents and young adults [4], and is a potential cause of low back pain. The mechanism of this pathologic process is indicated by experimental studies showing that the growth zone and the point of insertion of the annulus fibrosus into the vertebra are localised weak points [24].

Given its importance in the overall function of the disc, the end-plate appears to be a critical consideration in spinal reconstruction procedures. Current opinion regarding spinal fusion with either bone or implantable devices is that mechanical stability is essential, and accordingly such procedures require that the end-plate remains intact [50]. It has been claimed, however, that preservation of the vertebral end-plate does not offer a significant biomechanical advantage in anterior thoracolumbar column reconstruction, but rather that titanium cage constructs provide the greatest resistance to axial loads [17]. Such information is necessary for the appropriate design of devices to augment spinal fusions.

Any discussion of the end-plates would not be complete without reference to Schmorl's nodes. These lesions, which are found in over 70% of autopsy spines, are characterised by extrusion of the disc either cranially or caudally (or, in rare instances, both) into the vertebral body through a narrow aperture in the end-plate. The mechanism by which Schmorl's nodes form is unclear, but possible causes are trauma, tumour and congenital weakness of the cartilage resulting from the failure to heal spaces occupied by blood vessels during development. Schmorl's nodes are found with equal frequency above and below the age of 50 years and it seems unlikely that they occur as a result of disc degeneration [48] or vertebral bone density [16]. Rather, they are thought to predispose the disc to degeneration in later life. Schmorl himself attributed these lesions to foci of degenerate cartilage in the end-plate [39]. Indeed, scar tissue, presumably left over following regression of the nutrient vessels in earlier life, has been observed in the region of the end-plate [11, 47].

In conclusion, the end-plate is clearly an important part of a multi-component system. By careful observation and experimental design we now have a greater understanding of its many functions in the spine and can appreciate its importance in maintaining a healthy disc. The end-plate, like all other components of the spinal motion segment, is subjected to many physiological challenges that undoubtedly contribute to its failure. The challenge we face as scientists is to learn more about it so that we can confront the problems that arise due to this inevitable failure.

References

1. Aigner T, Gresk-Otter KR, Fairbank JC, von der Mark K, Urban JP (1998) Variation with age in the pattern of type X collagen expression in normal and scoliotic human intervertebral discs. *Calcif Tissue Int* 63:263–268
2. Anatoniou J, Goudsouzian M, Heathfield TF, Winterbottom N, Steffen T, Poole AR, Aebi M, Alini M (1996) The human lumbar endplate. Evidence of changes in biosynthesis and denaturation of the extracellular matrix with growth, maturation, aging, and degeneration. *Spine* 21:1153–1161
3. Ayad S, Weiss JB (1987) Biochemistry of the intervertebral disc. In: Jayson MIV (ed) *The lumbar spine and back pain*, 3rd edn. Churchill Livingstone, Edinburgh
4. Beggs I, Addison J (1998) Posterior vertebral rim fractures. *Br J Radiol* 71: 567–572
5. Bernick S, Caillet R (1982) Vertebral end-plate changes with aging of human vertebrae. *Spine* 7:97–102
6. Brinckmann P, Frobin W, Hierholzer E, Horst M (1983) Deformation of the vertebral end-plate under axial loading of the spine. *Spine* 8:851–856
7. Broberg KB On the mechanical behaviour of the intervertebral disc. (1983) *Spine* 8:151–165
8. Brown MF, Hukkanen MVJ, McCarthy ID, Redfern DRM, Batten JJ, Crock HV, Hughes SPF, Polak JM (1997) Sensory and sympathetic innervation of the vertebral endplate in patients with degenerative disc disease. *J Bone Joint Surg Br* 79:147–153
9. Carreon LY, Ito T, Yamada M, Uchiyama S, Takahashi H, Ikuta F (1996) Histologic changes in the disc after cervical spine trauma: evidence of disc absorption. *J Spinal Disord* 9:313–316
10. Carreon LY, Ito T, Yamada M, Uchiyama S, Takahashi HE (1997) Neovascularization induced by anulus and its inhibition by cartilage endplate. Its role in disc absorption. *Spine* 22: 1429–1434
11. Chandraraj S, Briggs CA, Opeskin K (1998) Disc herniations in the young and end-plate vascularity. *Clin Anat* 11:171–176
12. Crean JK, Roberts S, Jaffray DC, Eisenstein SM, Duance VC (1997) Matrix metalloproteinases in the human intervertebral disc: role in disc degeneration and scoliosis. *Spine* 22:2877–2884
13. Crock HV, Goldwasser M (1984) Anatomic studies of the circulation in the region of the vertebral endplate in adult greyhound dogs. *Spine* 9:702–706
14. Crock HV, Yoshizawa H (1976) The blood supply of the lumbar vertebral column. *Clin Orthop Rel Res* 115:6–21
15. Goupille P, Jayson MI, Valat JP, Freemont AJ (1998) Matrix metalloproteinases: the clue to intervertebral disc degeneration? *Spine* 23:1612–1626
16. Hilton RC, Ball J, Benn RT (1976) Vertebral end-plate lesions (Schmorl's nodes) in the dorsolumbar spine. *Ann Rheum Dis* 35:127–132
17. Hollowell JP, Vollmer DG, Wilson CR, Pintar FA, Yoganandan N (1996) Biomechanical analysis of thoracolumbar interbody constructs – how important is the endplate? *Spine* 21:1032–1036
18. Holm S, Maroudas A, Urban JPG, Selstam G, Nachemson A (1981) Nutrition of the intervertebral disc: Solute transport and metabolism. *Connect Tiss Res* 8: 101–119
19. Holmes AD, Hukins DWL, Freemont AJ (1993) End-plate displacement during compression of lumbar vertebra-disc-vertebra segments and the mechanism of failure. *Spine* 18:128–135
20. Hukins DWL (1988) Disc structure and function. In: Ghosh P (ed) *The biology of the intervertebral disc*. CRC Press, Boca Raton
21. Kanemoto M, Hukuda S, Komiya Y, Katsuura A, Nishioka J (1996) Immunohistochemical study of matrix metalloproteinase-3 and tissue inhibitor of metalloproteinase-1 in human intervertebral discs. *Spine* 21:1–8
22. Kang JD, Stefanovic-Racic M, McIntyre LA, Georgescu HI, Evans CH (1997) Toward a biochemical understanding of human intervertebral disc degeneration and herniation. Contributions of nitric oxide, interleukins, prostaglandin E2 and matrix metalloproteinases. *Spine* 22:1065–1073
23. Lammi P, Inkinen RI, von der Mark K, Puustjarvi K, Arokoski J, Hyttinen MM, Lammi MJ (1998) Localization of type X collagen in the intervertebral disc of mature beagle dogs. *Matrix Biol* 17:449–453
24. Lundin O, Ekstrom L, Hellstrom M, Holm S, Sward L (1998) Injuries in the adolescent porcine spine exposed to mechanical compression. *Spine* 23: 2574–2579
25. Maroudas A, Stockwell RA, Nachemson A, Urban J (1975) Factors involved in the nutrition of the human lumbar intervertebral disc: Cellularity and diffusion of glucose in vitro. *J Anat* 120:113–130
26. Moore RJ, Osti OL, Vernon-Roberts B, Fraser RD (1992) Changes in endplate vascularity after an outer anulus tear in the sheep. *Spine* 17:874–878
27. Moore RJ, Vernon-Roberts B, Fraser RD, Osti OL, Schembri M (1996) The origin and fate of herniated lumbar intervertebral disc tissue. *Spine* 21:2149–2155
28. Nachemson A, Lewin T, Maroudas A, Freeman MAR (1970) In vitro diffusion of dye through the endplates and the annulus fibrosus of human intervertebral discs. *Acta Orthop Scand* 41: 589–607
29. Natarajan RN, Ke JH, Andersson GB (1994) A model to study the disc degeneration process. *Spine* 19:259–265
30. Oda J, Tanaka H, Tsuzuki N (1988) Intervertebral disc changes with aging of human cervical vertebra from the neonate to the eighties. *Spine* 13: 1205–1211
31. Ogata K, Whiteside LA (1981) Nutritional pathways in the intervertebral disc: An experimental study using hydrogen washout technique. *Spine* 6: 211–216
32. Oki S, Matsuda Y, Shibata T, Okumura H, Desaki J (1996) Morphologic differences of the vascular buds in the vertebral endplate – scanning electron microscopic study. *Spine* 21:174–177
33. Pedrini-Mille A, Pedrini VA, Tudisio C, Ponseti IV, Weinstein SL, Maynard JA (1983) Proteoglycans of human scoliotic intervertebral disc. *J Bone Joint Surg Am* 65:815–823
34. Roberts S, Caterson B, Evans H, Eisenstein SM (1994) Proteoglycan components of the intervertebral disc and cartilage endplate: an immunolocalization study of animal and human tissue. *Histochem J* 26:402–411
35. Roberts S, McCall IW, Menage J, Hadaway MJ, Eisenstein SM (1997) Does the thickness of the vertebral subchondral bone reflect the composition of the intervertebral disc? *Eur Spine J* 6: 385–389
36. Roberts S, Menage J, Eisenstein SM (1993) The cartilage end-plate and intervertebral disc in scoliosis: calcification and other sequelae. *J Orthop Res* 11:747–757

-
37. Roberts S, Menage J, Urban JPG (1989) Biochemical and structural properties of the cartilage end-plate and its relation to the intervertebral disc. *Spine* 14:166–174
 38. Roberts S, Urban JP, Evans H, Eisenstein SM (1996) Transport properties of the human cartilage endplate in relation to its composition and calcification. *Spine* 21:415–420
 39. Schmorl G, Junghanns H (1971) *The human spine in health and disease*, 2nd Am edn. Grune and Stratton, New York
 40. Tanaka M, Nakahara S, Inoue H (1993) A pathologic study of discs in the elderly. Separation between the cartilaginous endplate and the vertebral body. *Spine* 18:1456–1462
 41. Taylor JR (1975) Growth of human intervertebral discs and vertebral bodies. *J Anat* 120:49–68
 42. Taylor JR, Twomey LT (1988) The development of the human intervertebral disc. In: Ghosh P (ed) *The biology of the intervertebral disc*. CRC Press, Boca Raton
 43. Twomey LT, Taylor JR (1987) Age changes in lumbar vertebrae and intervertebral discs. *Clin Orthop* 224:97–104
 44. Twomey LT, Taylor JR, Furniss B (1983) Age changes in the bone density and structure of the lumbar vertebral column. *J Anat* 136:15–25
 45. Urban JPG, Holm S, Maroudas A (1978) Diffusion of small solutes into the intervertebral disc. An in vivo study. *Biorheology* 15:203–221
 46. Urban JPG, Holm S, Maroudas A, Nachemson A (1977) Nutrition of the intervertebral disc. An in vivo study of solute transport. *Clin Orthop Rel Res* 129: 101–114
 47. Vernon-Roberts B (1987) Pathology of intervertebral discs and apophyseal joints. In: Jayson MIV (ed) *The lumbar spine and back pain*, 3rd edn. Churchill Livingstone, Edinburgh
 48. Vernon-Roberts B, Pirie CJ (1977) Degenerative changes in the intervertebral discs and their sequelae. *Rheumat Rehab* 16:13–21
 49. Wallace AL, Wyatt BC, McCarthy ID, Hughes SPF (1994) Humoral regulation of blood flow in the vertebral endplate. *Spine* 19:1324–1328
 50. Zindrick MR, Selby D (1996) Lumbar spinal fusion: Different types and indications. In: Wiesel SW, Weinstein JN, Herkowitz H, Dvorak J, Bell G, (eds) *The lumbar spine*, 2nd edn. Saunders, Philadelphia