Review

European Spine Journal

Eur Spine J (1993) 1:205–213

Intervertebral disc degeneration

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Dégénérescence du disque intervertébral

Résumé. La dégénérescence des disques du rachis humain est un phénomène complexe caractérisé par des modifications biochimiques affectant le nucléus pulposus et les couches profondes de l'annulus et l'apparition de fissures et de fentes irradiant de la zone centrale du disque vers sa périphérie. De plus, et sans doute indépendamment de ces phénomènes, apparaissent au niveau des couches superficielles de l'annulus, de petites désinsertions qui sont probablement des ruptures provoquées par les contraintes mécaniques. La présence de déchirures discales liées aux contraintes et dépourvues de tendance spontanée à la guérison, peut initier ou accélérer la dégénérescence de la zone centrale du disque. Nous postulons que la douleur d'origine discale peut être liée aux altérations présentées par la partie périphérique de l'annulus. Bien qu'il puisse sembler logique d'admettre que les disques présentant une hyperpression intradiscale prolongée puissent davantage être enclins à engendrer des douleurs reportées dans les couches superficielles de l'annulus, en raison d'une tension plus élevée, l'analyse des études prospectives n'a pas confirmé de relation entre la reproduction typique d'une douleur à la discographie et des valeurs élevées de pression intradiscale. On en conclut pour le moment, que les seules modifications morphologiques significatives apparaissant chez les patients présentant la reproduction d'une douleur typique à la discographie, sont des altérations diverses de l'annulus affectant ses couches superficielles. Il reste à établir s'il existe une certaine reproduction des fibres nerveuses pendant l'essai de réparation de ces défects.

Mots-clés: Dégénérescence discale – Disque intervertébral – Arthrose vertébrale lombaire – IRM – Discographie

Summary. Disc degeneration in the human spine is a complex phenomenon characterised by biochemical change in the nucleus pulposus and inner annulus and the formation of clefts and fissures radiating from the central area of the disc towards the periphery. In addition, and probably independent of these phenomena, discrete defects in the outer annular attachement are seen which are likely to be due to mechanical stress and failure. The presence of stress tears in disc tissue and their failure to heal can initiate or accelerate the degeneration of the central component of the intervertebral disc. We postulate that discogenic pain may be linked to damage to the outer portion of the annulus fibrosus. Although it would seem logical to assume that discs with sustained high intradiscal pressure would be more prone to pain referred in the outer annular layers because of higher tensile strain, analysis of prospective studies has failed to confirm a relationship between typical pain reproduction at discography and high pressure values. It is concluded that, at present, the only consistent morphological changes present in patients with pain reproduction at discography are the presence of various annular defects involving the outer layers. Whether nerve ingrowth during attempts at repair of these defects is a consistent feature remains to be established.

Key words: Disc degeneration – Intervertebral disc – Lumbar spondylosis – Magnetic resonance imaging – Discography

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A major obstacle in the attempt to define disc degeneration may lie in differentiating it from ageing. While the distinction between ageing and degeneration has potential importance, there is no means of distinguishing between the two (if indeed they are different) morphologically or biomechanically. The present article is an attempt at summarising the many historical contributions to the topic of disc degeneration and the experience gained from our own studies with an emphasis on the role of annular defects in the development of disc degeneration.

Pathology: historical development

The first description of the morphology of "internal derangement of the intervertebral disc structure" is from Schmorl and Junghanns [24]. They described the appearance of clefts extending from the nucleus pulposus into the annular layers in relation to the dessication of the disc characteristic of "intervertebral chondrosis". The formation of clefts was considered by Schmorl and Junghanns to be associated with the development of disc prolapse. Other discrete lesions of the annulus fibrosus were described in relation to osteophyte formation. These consisted of separation of the annulus from the vertebral body rim along a plane parallel and adjacent to the end-plate and seen specifically at the very periphery of the intervertebral disc.

In 1945, Coventry et al. [6] described the presence of concentric fissuring of the annulus as a typical feature encountered during the third decade of life. They postulated that these changes would precede those seen in the nucleus pulposus. Friberg and Hirsch [8, 9] in 1950 drew attention to the link between annular ruptures and disc degeneration as a separate entity from normal physiological ageing of the intervertebral disc. Three years later Hirsch and Schajowicz [13] described discrete changes of the annulus fibrosus which were seen as early as the second decade of life. These changes were characterized as mucous degeneration consisting of concentric cracks of varying sizes, more frequently seen in the posterior annulus and apparently not communicating with the nucleus pulposus. They were considered to be different from radial rupture which, in keeping with Friberg and Hirsch's earlier study, were seen to extend in an outward direction from the nucleus, more commonly in the posterior and posterolateral annulus of the two lower lumbar discs. Such ruptures were considered a consequence of mechanical pressure. It was also stated that, if such ruptures extended to the outer annulus fibrosus, "vascular connective tissue" was seen microscopically in and around the tear.

Morgan and King [17] in 1957 drew attention to the association between annular tears, radiographic instability and low back pain. They observed the presence of incomplete radial posterior tears in the lower lumbar segments and of anterior concentric fissures or slits in the upper lumbar spine, which they thought were a likely cause of instability.

Twenty years later Vernon-Roberts and Pirie [29], on the basis of their experience from over 300 lumbar spine autopsies, supported the observation of Schmorl and Junghanns of radiating lesions as extensions of clefts forming in the nucleus pulposus. On the evidence of the occasional vascular ingrowth around the margins of the clefts, it was suggested that clefts could extend into the annulus by a tearing process rather than by tissue breakdown due to a degenerative process. The presence of circumferential clefts within the annular layers, and of tears directed at right angles to the orientation of collagen bundles near the attachments of the annulus vertebral body (rim lesions), was confirmed. Hilton and Ball [12] in 1984 reported on the frequency, distribution and histological characteristics of rim lesions in 117 post-mortem spines. Rim lesions were often present within the anterior annulus and could be associated with major tears of the annulus fibrosus. Rim lesions frequently showed evidence of attempted repair, with fibrovascular and fibrocartilagenous tissue present in the region of the rim. On the basis of the histological appearances it was concluded that a traumatic aetiology was likely and that rim lesions could be relevant in the context of low back pain. Kirkaldy-Willis [15] postulated that radial tears could result from coalescence of small circumferential tears which could begin in the outer annulus fibrosus. His hypothesis linked repetitive trauma and degeneration in the sequence of events which lead to annular damage.

Morphological classification of annular defects

Based on material examined in the Bone and Joint Research Unit of the London Hospital, Division of Tissue Pathology, Institute of Medical and Veterinary Science, Adelaide and the Department of Pathology of the University of Adelaide, a classification of annular defects into three main types is proposed:

Type I: Rim lesions (annular tears) (Figs. 1, 2). These are defined as discrete defects of the outer annulus fibrosus, parallel and adjacent to one or both end-plates, and close to the insertion of the annular fibres into the bony vertebral rim. Rim lesions are frequently associated with ingrowth of vascular granulation tissue which may extend into the middle of the annulus. The adjacent bone may show a cup-shape defect; replacement of the marrow by granulation or fibrous tissue; sclerosis of the subjacent bony trabeculae; and osteophyte formation. Importantly, evidence of successful healing of rim lesions has not been recorded. They are rare in subjects under the age of 30 years, but increase in frequency thereafter, so that they are commonly encountered in the lumbar spine after the age of 50 years [12]. It is concluded that rim lesions are traumatic in origin, and may be the outcome of failure due to cyclic loading. Also, it is possible that the rim attachment may be affected by a degenerative process.

Type II: Concentric (circumferential) tears (Figs. 3, 4). These are frequently seen in the lateral annulus, but may extend both anteriorly and posteriorly. Especially when located in the outer layers, these lesions may be associated with vascular ingrowth. However, as with rim lesions, there is no histological evidence to suggest that successful healing takes place. As previously mentioned, circumferential tears are commonly communicated with rim lesions.

Type III: Radiating clefts (Figs. 5, 6). These are a common outcome of advanced degeneration. The clefts extend commonly from the nucleus pulposus to, or through, the outer lamellae of the annulus on a plane parallel or oblique to the end-plate. They particularly affect the posterior and posterolateral zones of the annulus,

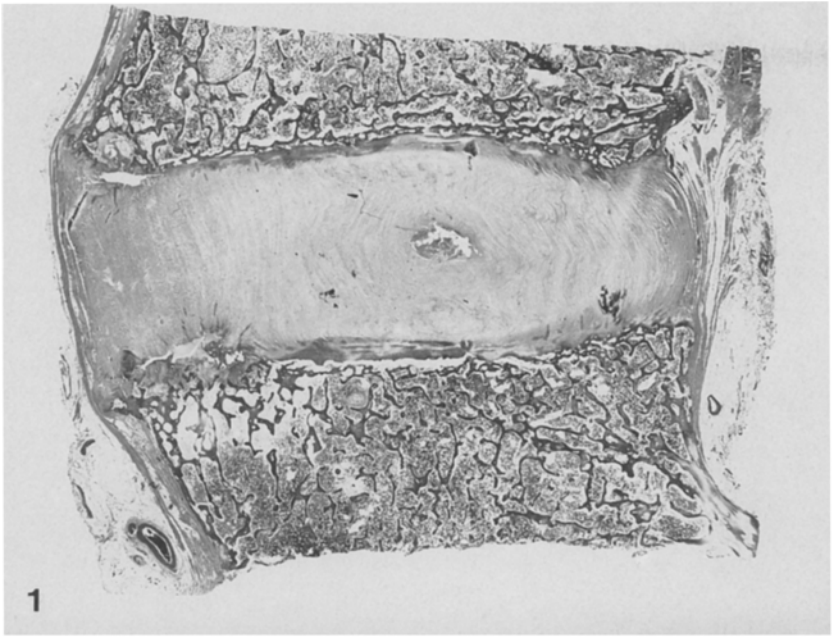

Fig. 1. Low-power micrograph of L2-3 intervertebral disc of a man aged 36. Rim lesions are seen in both the upper and lower end-plates

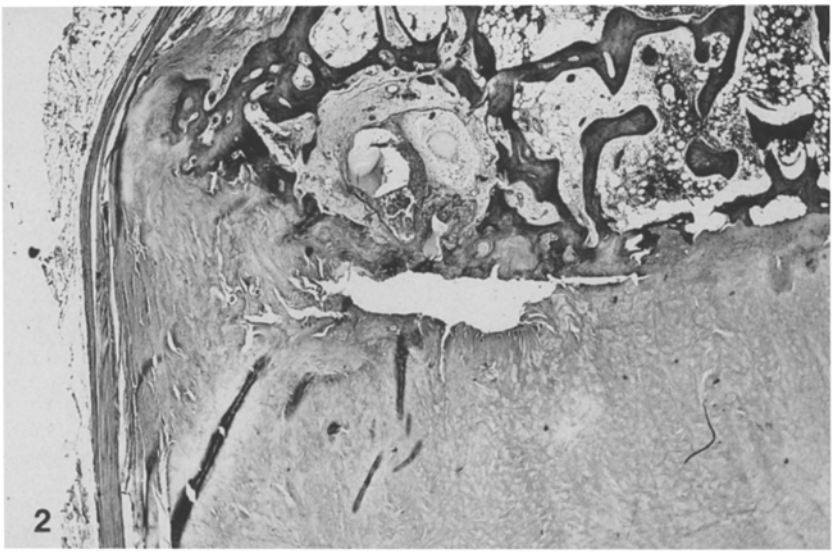

Fig. 2. High-power micrograph of lesion seen in Fig. 1. Replacement of bone marrow with granulation tissue adjacent to the annular lesion. Initial osteophyte formation is seen at the infero-anterior corner of the vertebral body, just proximal to the limit of the bony rim

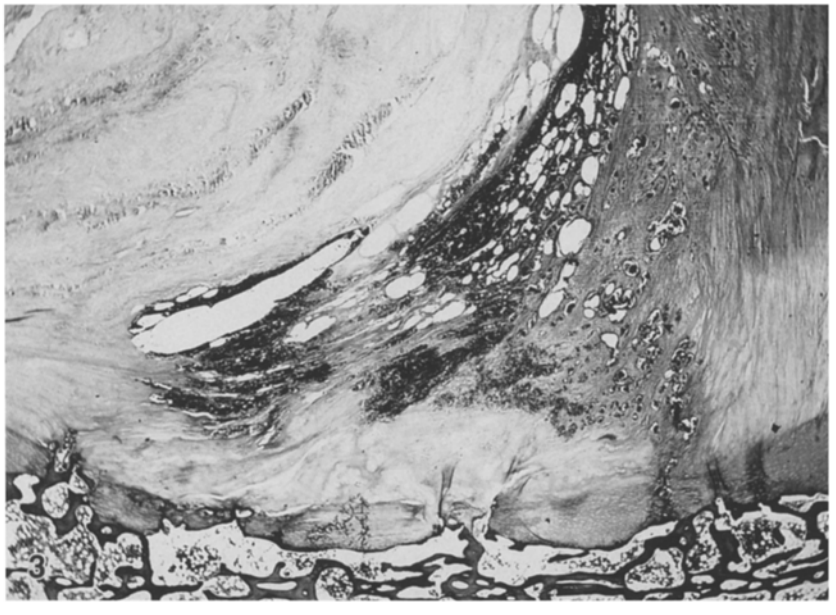

Fig. 3. High-power micrograph of L3-4 intervertebral disc of a man aged 60. An area of cystic degeneration associated with highly vascular granulation tissue is seen separating the central portion of the disc from the middle layers of the posterior annulus fibrosus

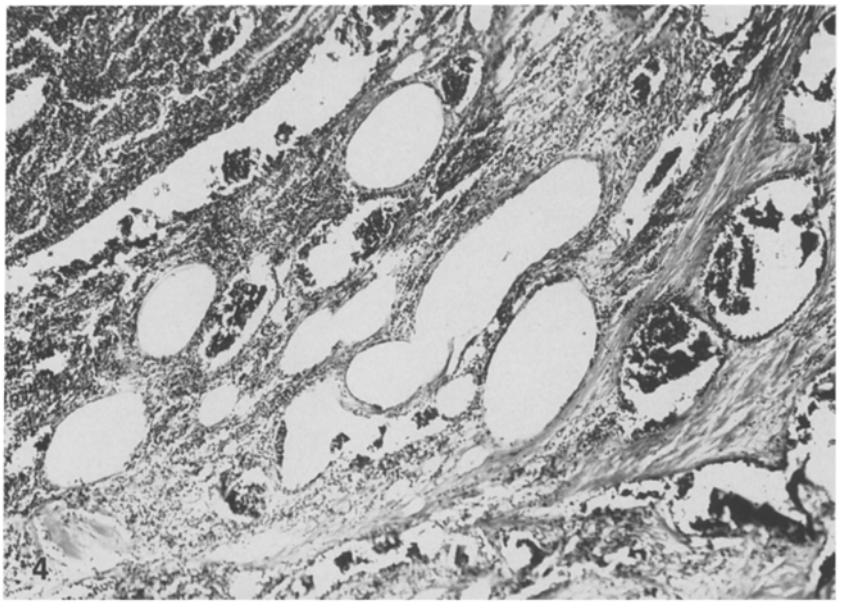

Fig. 4. Higher magnification of the lesion seen in Fig. 3. The characteristic cystic formation of highly vascular granulation tissue seen within annular tissue is well documented in this case

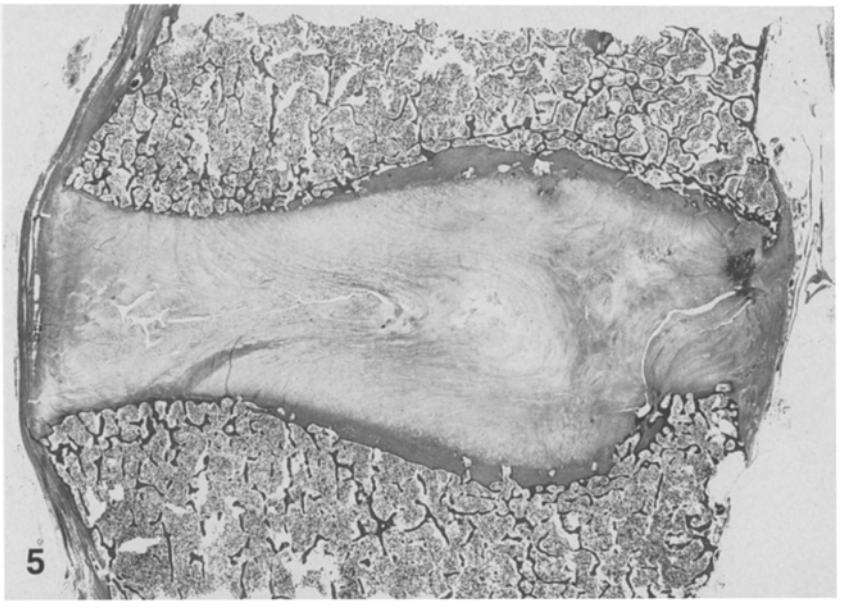

Fig. 5. Low-power micrograph of L4-5 intervertebral disc in a woman aged 50. An oblique cleft is seen in the posterior annulus fibrosus extending from the upper end-plate of the lower vertebra to the mid substance of the peripheral layers of the posterior annulus. The outer portion of the cleft is associated with marked vascularisation of the annulus

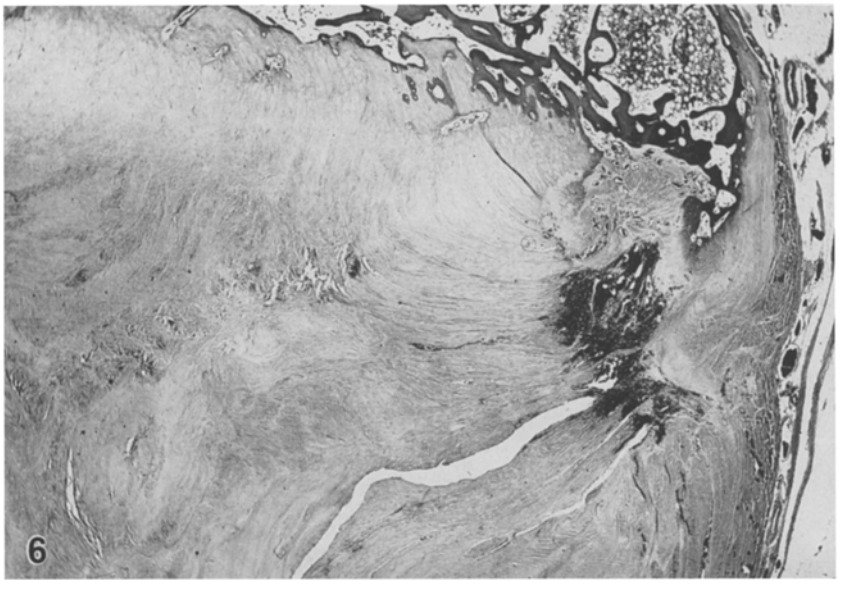

Fig. 6. High-power micrograph of the lesion seen in Fig. 5

Table 1. Summary of incidence of annulus tears (all subjects)

	Anterior annular tears			Posterior annular tears			Nucleus degeneration		
	Peripheral	Circum-ferential	Radiating	Peripheral	Circum-ferential	Radiating	1	2	3
L1-2	7	11	1	–	10	6	19	7	1
L2-3	6	12	–	3	13	3	17	9	1
L3-4	9	9	1	2	12	5	19	7	1
L4-5	12	12	–	3	13	6	15	11	1
L5-S1	4	7	2	5	18	13	9	13	5
Total no. of defects	38	51	4	13	66	33	79	47	9

although large clefts may extend anteriorly. Radiating clefts may be associated with nuclear displacement and form the pathway for the egress of nuclear and end-plate material, leading to disc protrusion and herniation. Posterior peripheral margins of radiating clefts frequently are vascularised, but successful healing is not encountered histologically.

Incidence of annular defects in the lumbar spine

To study the incidence of annular defects, 135 lumbar intervertebral discs from 27 spines removed at autopsy in Adelaide in subjects aged between 17 and 50 years were studied [22]. None had a history of trauma to the spine or had known skeletal or metabolic disorders.

The results are summarised in Tables 1 and 2. Peripheral tears were more frequently observed anteriorly, with the exception of the L5-S1 level where, out of nine rim lesions, four were seen anteriorly and five posteriorly. The distribution of circumferential tears was similar between the anterior and posterior annulus for the four upper levels, but in the L5-S1 disc 18 circumferential tears were seen in the posterior annulus, 7 anteriorly. Radiating clefts were almost exclusively seen in the posterior annulus, and were recent in almost half of the L5-S1 discs. Eight of the L1-2 discs had macroscopic evidence of nuclear degeneration compared with 18 of the L5-S1 discs. Radiating clefts were closely associated with the presence of nucleus pulposus degeneration.

Origin of annular defects

Our studies suggest that rim lesions involving the outer annulus fibrosus may occur in otherwise normal intervertebral discs, and may precede degenerative changes in other parts of the intervertebral joint complex. Moreover, on the evidence of their histological characteristics, it is likely that rim lesions result from mechanical failure of annular fibres rather than being due to biochemical degradation or some other degenerative process.

Galante [10] proposed that radiating ruptures formed as a combination of internal disc pressure and early failure of the inner annular fibres due to degenerative changes. This concept was challenged by Kirkaldy-Willis [15], who suggested that annular lesions would be first seen in the outer lamellae and would subsequently coalesce to extend inwards towards the nucleus pulposus. We believe that rim lesions involving the peripheral annulus fibrosus develop independent of radiating clefts that have been shown pathologically to form by projection of clefts which originate within the nucleus of ageing and degenerative discs [28]. The formation of discrete rim lesions in relatively young discs is almost certainly the result of mechanical failure of the peripheral annular lamellae consistent with the high tensile strain consequent upon the high intradiscal pressures which have been recorded [18, 19].

Table 2. Discs with no annular tears

	Patients under 35 years of age (90 discs)	Patients 35–50 years of age (45 discs)
L1-2	9	3
L2-3	11	3
L3-4	11	2
L4-5	6	2
L4-S1	8	2
Total	45	12

Degeneration of the disc and pain

The relationship between pathological changes of the intervertebral discs, outlined above, and back pain remains controversial. Kirkaldy-Willis [15] correlated degenerative changes of the intervertebral joints with the clinical presentation of patients suffering from back complaints. He divided the process of degeneration into the three phases: (1) dysfunction, (2) instability and (3) stabilisation. In the dysfunction phase, repetitive injury would result in interruption of normal function with early changes represented by circumferential and radial annular tears. In the instability phase, abnormal increased movements would be noted and would be characterised by laxity of the annulus. The progression of degenerative changes would result in the unstable segment regaining its stability through tissue fibrosis and osteophyte formation.

One of the reasons for the controversy surrounding the concept of discogenic pain is the fact that it has been clearly established that the "normal" (young and non-degenerate) disc has a nerve supply limited to the outer one-third of the annulus [2]. However, it has been reported that neuro-vascular ingrowth commonly occurs along the margins of radiating clefts, circumferential tears and rim lesions [28]. It has also been shown that nerve fibres capable of transmitting stimuli to pain may be present in the disc [27, 31]. Taking into account also reports that pain provocation during discography is associated with the presence of tears extending to the outer annulus [1, 20] and with neovascularisation of the disc, it appears probable that pain may originate from within the disc by virtue of the pathological changes.

Imaging

Discography

Since its introduction by Lindblom in 1948 as a means to diagnose disc prolapse, discography has been widely used in the assessment of patients with cervical and lumbar disc syndromes. Cloward [4] drew attention to the diagnostic value of discography in highlighting tears and disorganisation of the annulus fibrosus in the "ruptured lumbar intervertebral disc".

Nachemson [19] observed the relationship between intradiscal pressure, measured by the injection of fluid into the nucleus pulposus, and morphological patterns of discography. He concluded that significant differences could be found between discs classified as normal at discography and those interpreted as moderately or severely degenerate. In fact, moderate degeneration was associated with an increase of about 100% in the vertical load on the annulus fibrosus and a 50% decrease of tensile stress compared with normal discs.

Crock [7] drew attention to the phenomenon of typical pain reproduction by discography in patients with disabling back pain when the radiographic contrast pattern showed radiating clefts of the annulus. On the basis of extensive studies of end-plate vascularisation, he postulated that autoimmune mechanisms could play a relevant role in the development of the patient's symptoms. As a way of explaining the phenomenon of pain production following intradiscal injection, Brodsky and Binder [3] proposed that pressure transmitted through "a torn or weakened annulus" produced pain by stretching the annular fibres. In the same year, Park et al. [23] reported on 14 patients between 16 and 40 years of age with discographic evidence of posterior annular fissures extending backwards from an otherwise normally outlined nucleus. They postulated that radiating fissures of the annulus fibrosus could represent early evidence of disc injury. Two patients in their series failed to suffer pain reproduction during discography, and in both cases the pattern of contrast demonstrated complete radial rupture of the annulus with rapid extravasation of contrast into the epidural space. The authors explained this on the basis that pain provocation at discography would be the result of "transference of increased nucleus tension to the other annulus", which would not occur if a complete radial rupture was present. Adams et al. [1] correlated the pattern obtained by the contrast at discography on cadaveric material with five types of degeneration. They stated that discs with radiating clefts extending to the outer edge of the annulus, but with no leakage of contrast material into the epidural space, would be commonly found in patients with back pain and would most often be associated with symptomatic pain reproduction by the injection.

In a prospective study carried out in Adelaide [20] on 33 patients with 114 lumbar intervertebral discs investigated for low back pain, 36 of the 39 discs with typical pain reproduction at discography had tears extending to the outer annulus (Table 3). None of the 27 discograms showing a normal morphological pattern reproduced the patients' typical pain, and 24 did not cause any discomfort. Attempts at correlating intradiscal pressure values and pain did not demonstrate a definite relationship. While most of the discographically normal discs had high intradiscal pressure and no pain reproduction, three of the nine discograms of discs with low intradiscal pressure reproduced the patients' typical pain.

Magnetic resonance imaging

In recent years magnetic resonance imaging (MRI) of the spine has been used as a method of obtaining information on the state of the intervertebral disc. Gibson et al. [11] reported on a comparative study of 50 discs subjected to both MRI and discography. They concluded that MRI seemed to be more accurate than discography for the diagnosis of disc degeneration. This conclusion was based on the fact that four of the discs which were

Table 3. Correlation between pain reproduction, MRI and discography

Pain reproduction at discography	No. of discs	Patterns at discography				MRI signal intensity		
		Normal	Inner tear	Outer tear	Marked degeneration	Normal	Decreased	Absent
Absent	39	24	6	–	9	33	3	3
Atypical	36	3	15	6	12	15	18	3
Typical	39	–	3	27	9	12	18	9
Total	114	27	24	33	30	60	39	15

Table 4. Correlation between MRI and discography

MRI signal intensity from central zone of disc	No. of discs	Patterns at discography (discs)			
		Normal	Inner tear	Outer tear	Marked degeneration
Normal	60	27	15	12	6
Decreased	39	–	9	15	15
Absent	15	–	–	6	9
Total	114	27	24	33	30

reported normal at discography showed a decrease in the MRI signal from the nucleus pulposus. In one disc, however, the discography needle had been placed incorrectly in the annulus, and in the other three which had been reported as normal, lateral fissuring highlighted by the contrast material was present. The discrepancy between discography and MRI was attributed to an error of interpretation of the discogram.

Schneidermann et al. [25] reported on the correlation between MRI and discography in 101 discs from 36 patients, and concluded that MRI was accurate in predicting whether the disc morphology would be normal or abnormal at discography. However, they also stated that, based on signal intensity alone, the exact pattern of disc morphology seen at discography could not be determined by MRI. They added that, in patients with early acute symptoms due to acute herniation or tears in the annulus fibrosus, MRI may not show changes in signal intensity.

A recent in vitro study [30] correlated the signal obtained by MRI with the proteoglycan content of the intervertebral disc. A strong relation was found between signal intensity and water content of the tissue samples analysed.

In an experimental study of disc degeneration in sheep [21] in which a surgical lesion of the outer annulus fibrosus subsequently led to degeneration of the other components of the intervertebral disc, loss of signal at MRI was seen only after 12 months. This paralleled the dehydration of the intervertebral disc and the relative loss of aggregatable proteoglycan. These data also confirmed the experimental work of Lipson and Muir [16] of relatively higher hydration of the nucleus pulposus immediately following acute annular injury.

In the early phases of degeneration following substantial annular damage the nucleus pulposus may retain a relatively normal water content which is generally associated with high intradiscal pressure. This would apply specifically to stress-related injuries to the outer annulus. These findings should not be confused with the more common clinical situation of posterior disc prolapse, which is the outcome, usually, of advanced disc degeneration in which isolated fragments of nucleus, sometimes with attached cartilage end-plate and/or inner annulus, pass through radiating clefts involving the annulus (B. Vernon-Roberts, R. D. Fraser, and O. L. Osti, unpublished data, 1992). In this latter situation, disc prolapse would show marked alteration of signal intensity in T_2-weighted images. If, however, as in the case of the sheep model, annulus failure in the outer layers were present, MRI signal may fail to reveal any abnormality in intensity. It is only at a later stage that this would be highlighted by reduced or absent signal at MRI due to the relative change in proteoglycan content and disc water.

Zuckerman et al. [32] reported on a series of 18 patients in which MRI did not reflect internal disc morphology as outlined by discography. In all cases, despite MRI's being reported as being normal, discography showed tears extending to the outer annulus fibrosus with or without extravasation of contrast medium into the epidural space. The authors stated that discography may allow detection of significant pathology not suggested by MRI. They recommended that in patients with normal MRI and continuing symptoms, consideration should be given to further investigation by discography.

A prospective study carried out in Adelaide [20] compared MRI and discography in patients with discogenic back pain produced similar results (Table 4). Eighteen of sixty discs with normal signal intensity on MRI had marked degenerative changes demonstrated by discography. A further fifteen discs with normal MRI signal had annular tears in the presence of a well outlined nucleus pulposus. None of the abnormal discs, identified by MRI as having decreased or absent signal, showed normal morphological pattern on discography. These results suggest that, at present, discography offers a more sensitive evaluation of disc morphology than MRI, and provides valuable additional data on pressure and pain provocation. It is likely, however, that with the expected continuous improvement in techniques and enhancing contrast agents, MRI may in the near future be able to visualise annular defects in the presence of a normally hydrated nucleus pulposus. In addition, because of its very low false positive rate, MRI should at present be considered a valuable clinical screening modality in patients with discogenic pain.

Experimental studies

The idea of inducing experimental intervertebral disc degeneration by damaging the annulus fibrosus is not new. Key and Ford [14] used a dog model in which, through a transverse incision in the posterior longitudinal ligament and annulus fibrosus, immediate prolapse of nuclear material resulted. The authors noted that the defect in the annulus fibrosus tended to heal while the operative

defects in the deeper layers remained patent. On the evidence of these results, they suggested that the primary lesion leading to protrusion of the intervertebral disc may be a weakening of the posterior portion of the annulus fibrosus from degenerative changes or injury.

Smith and Wolmsley [26] used a rabbit model in which the annulus fibrosus was deeply incised anteriorly to obtain immediate nuclear prolapse. Their observations, in keeping with the findings of Key and Ford, suggested that healing occurred in the superficial lamellae of the annulus in association with a fibroblastic reaction typical of tissue healing in general. The failure of healing of the deep part of the wound was attributed to the recognised avascularity of the deeper annular fibres. The authors postulated that the presence of displaced nucleus pulposus separating annular lamellae would have had an additional influence against bridging of the defect. They observed extensive ossification of the ventral annulus in the animals sacrificed at longer time intervals after the operation. They postulated that, in humans, increasing pressure of the nucleus pulposus in association with movements of the spine and in the presence of initial degenerative changes may rupture the deepest lamellae of the disc.

Lipson and Muir [16] reported the biochemical changes during disc degeneration using the same rabbit model as described by Smith and Wolmsley. In all animals acute nucleus herniation was followed by secondary degenerative changes evidenced by metaplasia of the intervertebral disc into fibrocartilage and osteophyte formation at the site of the lesion. After early loss, the water content of the disc was rapidly restored 2 days after the operation. However, in the long term, progressive dehydration of the disc occurred in association with changes in the total uronic acid content. The authors suggested that loss of the confined fluid mechanics of the disc would appear to initiate the chemical changes seen in degeneration. They postulated that when a communication occurred between radial fissures and circumferential annular tears, a "concealed herniation would take place" which would then lead to irreversible mechanical damage and progressive degeneration.

A sheep model was developed in Adelaide [21] to test the hypothesis that discrete peripheral tears within the outer annulus fibrosus lead to secondary degenerative changes in other disc components. The results of these experiments demonstrated that despite great care being taken to ensure that the inner annulus was not involved in the initial lesion, progressive failure of the inner annulus took place between 4 and 12 months after operation. While healing of the outer annular defect occurred, no evidence of repair was seen in the inner portion of the original cut. Of the biochemical parameters examined, disc proteoglycans, proteoglycan aggregation and matrix protein levels were significantly changed in the operated discs and were consistent with progressive disc degeneration [5]. The result of this sheep study indicated that discrete tears of the outer annulus may have a role in the formation of concentric tears and accelerating the development of radiating clefts and degeneration in the disc. It was concluded that localised peripheral tears may be relevant to the pathogenesis of the early phases of degeneration of the human intervertebral disc and in the production of discogenic pain.

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