Clinical importance of the intervertebral disc, or back pain for biochemists

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Abstract
The object of this paper is to give biochemists some insight into current thinking on back pain. I shall discuss the important, but limited, relationship of back pain to the principal pathological changes in the lumbar intervertebral discs. I shall point out some of the areas where scientists may be able to help clinicians understand and treat this common, but complex, condition. The literature on back pain is enormous, so I have made no attempt to select even a small part of it for this article.

Epidemiology/economics
Back pain affects 60–80% of us at some time in our lives. Mostly these attacks are short-lived and self-limiting, but about 5% of adults have chronic or recurrent back pain. The direct annual costs to the UK health service (£1632 million) and the indirect costs of back pain to society (£10668 million) are enormous [1]. This is one of the most costly conditions that afflicts us. In spite of these high costs the involvement of disc biology in back pain has been a low priority for research investment. A recent PubMed search found that the number of papers published on disc biology is only around 10% of the number published on biology of articular cartilage and less than 0.5% of those published on kidney biology.

Anatomy
The spine consists of vertebrae, each connected by three joints. The main joint is the intervertebral disc. Two posterior guiding joints vary in orientation in different parts of the spine. The disc has a tough outer layer of laminated fibres (the annulus) which contains a softer centre (the nucleus). It is the largest avascular structure in the body (the next largest is the lens of the eye). Details of its structure and function are to be found in accompanying articles in this colloquium.

Causes of back pain
The cause of most back pain is unknown. Disc degeneration occurs in a similar pattern to back pain and is implicated in most types of back pain. Muscle control, or rather the lack of it, is disturbed in most back pain sufferers. The control system for the postural muscles is complex and poorly understood. It is likely that some pain arises when this system is disturbed. This occurs when there is a mismatch between expected and observed activity. Most therapeutic regimes focus on restoration of muscle function and whole-body rehabilitation. There is strong evidence for the efficacy of fitness programmes for back pain.

Chronic pain is complex and does not always reflect tissue damage. Pain can be affected by personality, depression, secondary gain through litigation as well as many other unknown factors. Pain that persists alters the physiology of the afferent nerve fibres and relay cells in the dorsal horn of the spinal cord and then right on through the nervous system to the cerebral cortex.

Classification
There are many clinical classifications of back pain. One fairly simple scheme is to consider five types of presentation or syndrome. I have given a brief description of the possible relationship of these to disc degeneration.

Type I
This is the commonest. Usually attacks are short-lived. Disturbance of muscle function is implicated and disc degeneration is probably

Key words: back pain, intervertebral disc degeneration, spine.

Abbreviations used: MRI, magnetic resonance imaging; CT, computed tomography.

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irrelevant. Treatment is by fitness and exercise programmes. Manipulative therapy may help but is superimposed on a background of self-resolution.

**Type 2**
This is the chronic type and extends in a spectrum of severity from type 1 back pain. Pain may be severe and resolves slowly, if at all. Again, muscles are dysfunctional, but disc degeneration is implicated in some patients. This may be because the disc is intrinsically painful or because normal movement between the segments is disrupted. Sometimes this is called instability, although it is unusual for this to fulfill a mechanical definition of the term. This may in turn affect muscle function. Treatment is by rehabilitation and occasionally surgical fusion.

**Type 3**
This is nerve root pain and back pain. The common cause is intervertebral disc herniation. This requires a combination of disc degeneration, disc fragmentation and a tear in the annulus. Fragments of disc are extruded. Most commonly this is into the spinal canal. The nerves within the canal are vulnerable to a combination of compression and chemical inflammation. The extruded disc contains cytokines which contribute to this process. The amount and type of pain varies considerably from one person to the next. Up to 25% of adults have some evidence of disc herniation. Not all are painful. The natural history of a symptomatic herniation runs from back pain to lower limb pain over a variable time scale. Most resolve. Those that do not can be treated by surgical excision. This is usually effective in relieving leg pain, but not back pain. In my opinion, manipulation should be avoided when there is significant root pain. Disc herniation can compress the whole cauda equina if the herniation is very large, central or in the presence of a narrow vertebral canal.

**Type 4**
This is walking-related back and leg pain known as neurogenic claudication. The pain is reduced by leaning forward, sitting or squatting. The severity varies from trivial to grossly disabling with the inability to stand or walk for more than a minute or two. Here there is chronic, and sometimes evolving, narrowing of either the vertebral canal, lateral recesses and or exit foramena. This may be a developmental stenosis which might be of unknown origin or associated with achondroplasia, which is the commonest cause of short stature. More likely is that the stenosis is acquired by disc degeneration leading to a combination of narrowing, bulging and herniation. This deforms the segment and leads to secondary degenerative changes in the facet joints which in turn throw out bony osteophytes. The ligaments between the vertebrae (especially the ligamentum flavum) tend to crumple and deform. This leads to a characteristic syndrome mainly affecting people in middle age or the elderly. Treatment is by advice, analgesia or surgical decompression.

**Type 5**
This is where there is back pain caused by serious pathology, such as by cancer, infection or fracture. This is fortunately the least common cause of back pain, but a diagnosis that doctors are anxious to exclude. Patients less than 18 and more than 55 years are the most likely to present with back pain with a serious underlying cause. Disc degeneration is not implicated in this group of patients.

**Detection of disc degeneration**
Disc degeneration is implicated in various ways in back pain of types 2, 3 and 4. It can be detected by a variety of techniques.

**Post mortem**
The classic studies of disc pathology were made in post-mortem discs by Schmorl and Junghanns in Germany in the 1920s and 1930s [2]. This is not a good way of obtaining epidemiological data on back pain, which is, of course, not a fatal condition (except through suicide which does occur in chronic pain patients). Also, post mortems are now less commonly performed, and disc material is difficult to obtain for research.

**X-rays**
X-rays of the lumbar spine show changes in more severe stages of disc degeneration. Large cross-sectional studies were done in the 1950s and 1960s by Kellgren and Lawrence [3]. These showed an increasing incidence of disc degeneration with age, and a higher proportion of more severe changes in symptomatic populations. It is no longer ethical to X-ray asymptomatic patients.

**Magnetic resonance imaging (MRI) scanning**
This is now widely used and there are classification systems. Mostly data have been acquired from patients with symptoms, but there are some small surveys of asymptomatic patients suggesting that changes observed by MRI are common. A small,
but important, prospective study by Boos et al. [4] showed that disc degeneration in asymptomatic adults did not predict back pain in a 5 year follow-up window. This is in contrast with 14-year-old asymptomatic adolescents with disc degeneration who were much more likely to have back pain by age 20 than MRI normal controls [5].

**Discography and computed tomography (CT) discography**
This method is unpleasant and involves injecting contrast into the disc. This shows patterns of degeneration and annular tears on plain X-ray or CT. This method also provokes pain much more in degenerate discs than in ‘normal’ discs. Unfortunately there is a lot of noise through difficulties in interpreting the patient’s response to the injection and the method remains controversial.

**Animal models**
There is no really good animal model of disc degeneration. Although discs are found in the spines of the earliest vertebrates, there are subtle, but important, interspecies variations. There are mammalian lines with tendencies to degenerative changes. However, for the small number of studies in this area, researchers have mainly relied on mechanically induced disc degeneration in large mammals (a small scalpel wound in the annulus); this may well not accord with humans. One problem is that humans are bipedal, another is whether or not the degenerate animal disc causes pain.

**What do clinicians want to know from scientists about the intervertebral disc?**
Below is a list of areas that clinicians want to know more about from scientists with respect to the intervertebral disc.
- Anatomy and microstructure;
- Mechanisms of (i) disc degeneration and (ii) cytokine production and release from degenerated and herniated discs;
- Cell products and the patterns and mechanisms of their production;
- The biochemical response to mechanical and ischaemic stress;
- Why nerves and blood vessels grow into degenerate but not normal discs;
- Genetic mechanisms involved in disc degeneration and pain production;
- Possibilities for the reversal of degenerative processes.

**References**

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