

# Pathophysiology of disc degeneration

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Disc degeneration implies a deterioration of the physical and chemical properties of the whole tissue or parts of the structure with frequent pathological changes in the cells or macromolecules. The consequence of this degenerative process will, in most cases, result in destruction or inhibition of function, either as regional abnormalities or subsequently as mechanical disorders of the motion segment, thus affecting the whole spine (Nachemson 1976). Unfortunately, a causal relationship between the disc degenerative process and low back pain is not yet established (Magora and Schwartz 1976). Although the intervertebral disc undergoes age changes over time, which can be defined as morphologic anatomical events, degeneration is often associated with clinical complaints or additional cellular disturbances producing an unpredictable pathophysiological tissue arrangement, which is necessarily neither age dependent nor entirely irreversible. Progressive changes in the disc architecture such as fibrosis, loss of the gelatinous character of the nucleus pulposus, coarsening of the anulus fibrosus fibers, change of demarcation between anulus and nucleus and deposition of pigments constitute the aging procedure. Several of these changes have considerable impact on the nutrition of disc, especially, when nutrient canals and spaces in bone adjacent to the endplate cartilage are usually partly or completely occluded in specimens from individuals in the fourth decade of age. Furthermore, aging also affects the peripheral microvasculature, demonstrating a thick basement membrane thereby reducing the transport capacity through the capillary wall (Ballard et al. 1979, Bernick and Cailliet 1982). The distinction of natural age-associated changes in the disc tissue and degenerative processes is complicated by the individual variability in spinal mechanics and efficiency of the various physiological functions within the body.

## Transport properties

The adult disc is avascular; therefore nutrients can be supplied to and waste products removed from the disc cells only by transport through the disc matrix (Figure

1). Changes in the microcirculation around the disc can dramatically affect the fluid flow pattern within the disc. Among all the possible functions that might alter the rheologic system, and thereby affect transport and metabolism of the disc cells, various models of exercise seem to be important. First, during prolonged exercise as well as under prolonged external load, the disc deforms and loses fluid. The change in disc dimensions may affect the concentration of nutrients in the center of the disc. Exercise may also affect the peripheral circulation in several ways and hence alter the rate at which metabolites reach the disc interface (Holm 1990). Secondly, by introducing external factors that may disturb the circulation, such as smoking, vibration, or specific medical treatment, the nutrition of the disc may be affected. Finally, motion of the disc system itself changes the concentration of blood solutes such as lactic acid and glucose and may affect pH. These external changes may also influence the concentration of such substances in the disc itself. However, in the normal disc, these changes would be expected to be immediate and reversible. In degenerated discs, the transport function may be disturbed to such an extent that there is no adequate immediate reversible transport function. In contrast, a prolonged period of exercise, or alternatively, a prolonged period of immobilization of a disc segment, appear to have a dramatic and permanent influence on the transport of nutrients into the disc (Holm 1990).

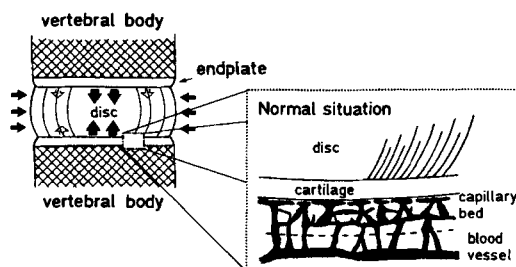


Figure 1. Nutritional routes into the intervertebral disc, arrows indicating the magnitude of solute transport. The enlarged view shows the capillary bed underneath the vertebral endplate.

Table 1. Factors that affect the concentration of nutrients in the disc tissue

Diffusibility within matrix
Disc thickness
Blood vessel contact area
Cellular demand
Cell density
Cell activity

### Cellular metabolism

The mechanical function of the intervertebral disc depends on the characteristics of the tissue matrix. The cells of the disc are responsible for renewing and repairing the matrix constituents. Matrix synthesis in the disc involves several pools of proteoglycans and collagens which normally turn over at different rates to fulfill the energy demands in various parts of the tissue. When the tissue undergoes degenerative processes, the synthesis rate is in general considerably reduced. The cellular surrounding tends to be "poisoned" by extracellular components, which do not enable the cells to keep a high synthesis rate. The removal of these poisoning constituents thus enhance the cellular function and eventually establish normal solute gradients.

Also, the size and avascular nature of the disc as such create concentration gradients for metabolites (Table 1). Such conditions apply to oxygen, glucose, sulphate and some other essential molecules, when the rate of consumption is large compared to the rate of solute transport to the cell. Steep gradients also exist for end products like lactate (Holm 1990). The high lactate levels found in the central part of degenerated discs must be associated with the lowering of the pH, which in turn are triggering and activating the proteolytic enzyme system (Holm and Nachemson 1982). The intervertebral disc contains many different proteases; collagenase and elastase have recently been found (Sedowofia 1979). Also, a system for protease inhibitors has been extracted from the human intervertebral disc. It is however evident, from the degradation of newly formed proteoglycans, that some degrading enzymes systems are present in the intervertebral disc matrix (Oegema et al. 1979). In the healthy disc there is likely to be a delicate balance between the active and the latent forms of enzymes and the potency of the inhibitors present; this balance could be very pH sensitive, and hence a change in the disc metabolism, which decreases pH could lead to a rapidly accelerating matrix break down.

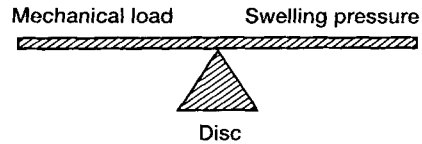


Figure 2. The intervertebral disc is balancing the mechanical load by molecular swelling pressure. During the upright position the mechanical load is higher than the swelling pressure but in a supine position the swelling pressure will dominate.

### Macromolecular arrangements

The arrangement of the collagen network of the disc consists of a series of concentric lamellae that encircle the disc and constitute the anulus fibrosus. These lamellae consist of collagen fibrils arranged in bundles that run obliquely between the adjacent vertebral bodies and are firmly anchored to them. The nucleus does not have such an organized collagen network; the fine fibrils of the nucleus form a loose irregular mesh, which hold a large amount of the water binding proteoglycans, hence creating a swelling pressure. This important constitution, together with the ability of molecular aggregation, enables the tissue to withstand pressures resulting from external loading (Figure 2).

Although the water content decreases with age, the substance remains an important component of both old and degenerated discs. The water content of the disc is not constant, but varies with applied load, thereby also undergoing a diurnal variation. Because of the low cell content, most of this water is extracellular and is associated with the collagen and proteoglycans (Figure 3). A significant proportion of the water in degenerated discs with low proteoglycan content may be intrafibrillar. This intrafibrillar fraction of water is freely exchangeable, but is not available to the proteoglycans (Urban 1990). Because of the negative charges on the macromolecules, the total number of ions in the tissue is always greater than in the plasma. Osmotic pressure of the disc results from a difference in number of soluble particles between the two phases; the excess num-

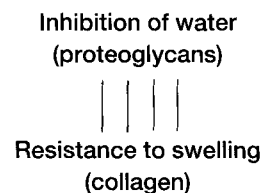


Figure 3. A delicate balance exists between the action of the macromolecules in the disc. The proteoglycans imbibe water until the collagen fibers apply too strong of a resistance. At equilibrium, the two forces are equal.

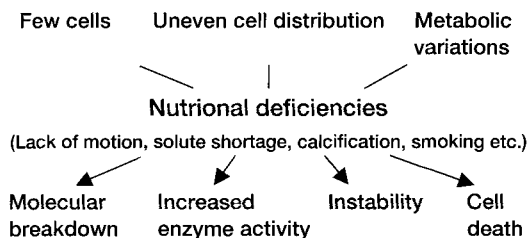


Figure 4. With age the inevitable result for the intervertebral disc will be nutritional deficiency. On top of that, degenerative factors will contribute, and together age and degeneration create a destructive flow of events.

ber of ions in the tissue leads to the high osmotic pressure of the disc. A further very important osmotic feature is the size and shape of the aggregating proteoglycans. This concentration of proteoglycans also determines the partition of various ions. Cations are more highly concentrated in the tissue than in the surrounding plasma, whereas anions are less concentrated because they are excluded by the fixed negative charges present on the proteoglycan side chains (Urban 1990). Calcium content is, of course, important for both normal and pathological calcification and hence will be influenced by proteoglycan concentration.

Changes in the macromolecular composition of the disc have been characterized for a few pathological conditions, like scoliotic discs, spondylolisthesis, enzymatically degraded discs, fused discs and in experimental models of variable disc lesion approaches.

If the disc and collagen network are injured, full function cannot be restored without renewal of this framework. Furthermore, the mechanical function of the disc will be impaired until the proteoglycans are anchored in the tissue and the molecular aggregation and thus the water binding capacity is optimized.

### *Pathophysiologic implications*

The mechanical function of the intervertebral disc depends upon the integrity of the disc matrix. The matrix is produced and maintained by the cells of the disc; thus, the health of the tissue depends to a large extent on the viability of these cells. By changing the nutritional supply to the cells or introducing mechanically or chemically unfavorable functions to the disc system, degenerative processes may be introduced (Figure 4). These processes may change the tissue characteristics in many ways, mostly reducing tissue flexibility, transport efficiency or cellular capacity. The inevitable consequence over a longer period of

time will be an unhealthy cascade of events including enzymatic degradation, instability, nerve reactions and probably back pain.

### References

- Ballard KW, Bernick S and Soben S S. Changes in the human microcirculation with age. *Microvasc Res* 1979; 17: 511-514.
- Bernick S, Cailliet R. Vertebral endplate changes with aging of human vertebrae. *Spine* 1982; 7: 97-102.
- Holm S, Nachemson A. Nutrition changes in the canine intervertebral disc after spinal fusion. *Clin Orthop* 1982; 169: 243-258.
- Holm S. Nutrition of the intervertebral disc. In: *The lumbar spine* (Eds. Weinstein J N and Wiesel S W) WB Saunders Company 1990: 244-260.
- Magora A, Schwartz A. Relation between the low back pain syndrome and x-ray findings. *Degenerative osteoarthritis. Scand J Rehab Med* 1976; 8: 115-125.
- Nachemson A. The lumbar spine. An orthopaedic challenge. *Spine* 1976; 1: 59-71.
- Oegema T R, Bradford D S, Cooper K M. Aggregated proteoglycan synthesis in organ cultures of nucleus pulposus. *J Biol Chem* 1979; 254: 10579-10581.
- Sedowofia S K A, Tomlinson I, Jayson M I V, Weiss J B. Identification of collagenase and other neutral proteinases in human intervertebral disc. *Ann Rheum Dis.* 1979; 38: 573-592.
- Urban J. Disc biochemistry in relation to function. In: *The lumbar spine* (Eds. Weinstein J N and Wiesel S W) WB Saunders Company 1990: 231-244.