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## Gonstead Disc Model Revisited Pt.III

# Intervertebral Disc Nutrient Transport: A Literature Review

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The intervertebral disc is fascinating in its complexity. Despite over 100 years of research by cadres of researchers who have studied its structure and function and after untold numbers of surgical interventions, there is still much that is contentious, poorly understood, and unknown. What is amazing is how a single chiropractor from a rural community in Wisconsin developed a remarkable understanding of the function of the intervertebral disc and was able translate it into a means to help so many people with severe disc injury. Part III summarizes the research findings to date on the transport mechanism of nutrients into and waste products out of the intervertebral disc (henceforth "disc"). Like Dr. Gonstead, we must keep current by studying the spine and disc extensively. In this way, we can better help people who seek our care.

As we know, the mature disc is largely avascular and requires an indirect system to supply nutrients for processes, such as, glycolysis and to remove waste products, such as, lactic acid. This process is also necessary to regulate the proper pH to maintain the physiological processes that the disc cells require. In addition, many of the cells in the disc live a precarious existence by being far removed from their nutrient source. To maintain the health of the disc requires an efficient supply chain that is considerably more intricate and critical than the "just-in-time" supply stream of modern-day manufacturers.

Almost all of the studies were done on the lumbar spine. Unstated is if there are significant differences in the thoracic or cervical spine, or for that matter, in the unfused sacrum or coccyx intersegmental spaces.

### Nutrient Supply to the Disc

There are two avenues for disc nutrient transport and waste removal, both of which utilize a complex system of arterial and venous blood flow to bring in nutrients and remove waste. Glucose, oxygen, and other necessary materials are brought in. Lactic acid and other waste products are eliminated. The process occurs through either the vertebral cartilaginous endplates or the vascular network that surrounds the periphery of the disc. (1,2,3,4,5) The primary avenue is through the vertebral endplates. Transport through the endplates supply the nucleus pulposus and much of the anulus fibrosus as the central region of the nucleus may be up to 20 mm from the nearest blood vessel. (3) The outermost anulus is supplied by blood vessels in the paradiscal soft tissues. (4,6)

The two physiological processes that facilitate nutrient transport into the disc are diffusion and fluid convention. Fluid flow transports large molecules, and diffusion is effective at transporting smaller molecules. (1) Diffusion through a concentration gradient appears to be the primary process, and it allows passage of small solutes such as glucose and lactic acid, and possibly oxygen. (2,4,6) Nobody knows the exact mechanism through which oxygen is brought in. Fluid convection appears to be the secondary system and, unlike diffusion, is affected by diurnal loading patterns (6) and movement. (5) As we know, on a diurnal basis, the disc swells and contracts with the spine lengthening and shortening. Adams and Hutton found that posture made a difference in flow into the disc. Flexion caused a greater outflow of fluids from the disc than erect neutral or extended posture. Unloading, reversed the trend and causes the diurnal changes in disc height. (1)

The shape, size and fixed charge of the molecules that are attempting to pass through the has an affect on their ability to pass through the endplate cartilage. Long chain molecules pass through with difficulty, particularly if the density of the constituents of the cartilage is high. (33)

The interplay of extracellular oxygen and pH is critical. Disc matrix synthesis is greatest around 5% oxygen and is markedly inhibited below 5%. (6) Matrix synthesis is greatest at a pH of 7.0 and drops steeply in a more acidic pH level. Cell death occurs in a low or acidic pH. (6) Glucose is the primary nutrient of the disc and is vital for glycolysis, the process to create adenosine triphosphate (ATP) production. (6) A drop in glucose concentration below 0.2 mM causes cell death. (6)

There is a complex interplay between the fluid volume and the matrix in the disc. The matrix is composed of collagen fibers and proteoglycans in solution – 65%-90% of volume of the disc is water – and is important for load-bearing. (7) In the high osmotic pressure of the solution, electrolytic proteoglycans are hydrophilic and can imbibe a significant amount of water. (7, 34) The negatively charged glycosaminoglycan or GAG – chondroitin sulfate and keratan sulfate (the former is more negatively charged and more hydrophilic than the later (8) – is the key factor in maintaining osmotic pressure in the matrix. (7) In this way, a chemical pump is formed that can move water and small solutes through fine pores in tissues. The propensity of hydrophilic proteoglycans to bring in fluids and solutes is balanced by the collagen network or matrix which slows the process when it is in tension. (34) The nucleus pulposus has a greater water content and fixed charged density than the outer anulus fibrosus. (7) Maroudas states that GAG is the “business part” of the proteoglycan while the other constituents are structural components. (7) This topic of the biochemical constituents of the disc will be covered in a future part.

**Nutrients**

The primary nutrient required by the disc is glucose which maintains the viability of disc cells. A product of glycolysis is lactic acid. Efficient disc transport is required to supply glucose and remove lactic acid as reduced glucose concentrations and the accumulation of lactic acid leads to disc cell death. (9) The normal disc has a pH of 6.9 to 7.0, but it can became very acidic if excess lactic acid is not removed; it can be down to pH 6.1 in pathological states. An overly acidic environment inhibits cell metabolism. (10) Oxygen is also very important for disc cell viability. When oxygen levels are low, the production rate of various macromolecules in the disc is reduced. (6)

The efficient supply of nutrients is very critical as some disc cells may be as far as 5 to 8 mm or more from the nearest blood supply. (3,4,7) To reach all of the cells requires concentration gradients and a convection current such as that produced by movement. (7)

**Peridiscal Nutrient Supply**

There is an extensive vascular supply that surrounds the outer layer of the anulus fibrosus. Most appear to be on or near the surface of the outer anulus, but some may penetrate 1-2 mm into the disc. (10) In the mature disc, it appears that oxygen, glucose, amino acids, and sulfate passes from the small, perianular blood vessels to the disc. (9) In the fetus and infant, there is blood supply entering the outer third or half of the anulus. These are largely gone in the mature disc. (11)

Blood vessels have been found in damage regions of injured discs and accompany nerve fibers that penetrate the disc into these regions. The purpose of this vascular supply is unknown. (12)

**Vertebral Endplate Nutrient Transport**

The vertebral endplates are a thin margin between the vertebral body and the disc. They are considered to be part of the disc rather than the body. The endplates are about 0.6 mm (0.5 to 1.5 mm) thick and are thinnest in the central region over the nucleus pulposus. (13,14,15) A cross-section of the vertebral endplates begins with the subchondral bone of the vertebral body, a deep calcified layer, and a hyaline cartilage layer. (165) The biochemical constituents of the endplates are similar to the disc and consists of proteoglycans, collagen, and water, the former two are similar in concentration to articular cartilage. (14)

The vertebral body is richly bathed in blood. Capillary buds pass through marrow contact channels through the mineralized endplate and stop at but do not penetrate the cartilaginous endplate. (16) From blood vessels in the posterior aspect of the vertebral body at the waist of the body, three sets of blood vessels branch off. One enters the vertebral body and anastomose throughout the centrum. Another branch passes upwards towards the superior body, and the third travels towards the inferior body. (11,17) the multiple branches surround the vertebral body with vascular vessels.

The vertebral body marrow has also been found to contact the cartilaginous endplate. (14) In the past, marrow contact with the endplates were called "vascular buds" or "marrow contact channels." (14,18,19) Both contact by blood vessels and the marrow to the endplate is greater in the central region. (14)

In the infant, there is an extensive capillary bed in the developing vertebral endplate. These capillaries end in bulbs. In the adult, the extensive capillary canals are in the cartilaginous endplates.(11) Capillary terminations in the endplates, which appear like suckers on an octopus' tentacles, are larger and more densely concentrated in the central region over the nucleus pulposus. (2,20,21) The highest degree of permeability, and therefore nutrient exchange, is in the central region. (9,16,21) The endplate capillaries which arise from a variety of diverse arterial sources and drain into a complex of veins that proceed to the spinal canal. (17) The venous drainage has two systems, one goes up into a complex of veins in the vertebral body marrow while the other, in the mature spine, is a subarticular horizontal collecting system that disperse in various directions before exiting the vertebral body. The latter system is associated with certain disc disorders that can be viewed on MRI. (20,21) The venous outflow passes into Batson's plexus. (20) [*see figure on p.6*]

Smaller molecules can usually pass through the endplate more easily than larger ones. The charge of the solute, as well, affects the ability to pass through the endplate. A relatively large, positively charged solute, such as lysozyme, can pass relatively easily. The shape of a solute can also affect the ease of passage. Changes in proteoglycan levels through it, which acts like a regulator flow and acts like variable "pore size" mechanism, in the disc matrix affects the transport mechanism. (15,34)

**Disc Fluid Ingestion**

White and Panjabi hypothesize that acute, post-traumatic, lower back pain and muscle spasms may be due to a rapid ingress of fluid into the nucleus pulposus – this is undoubtedly the Gonstead acute D1 "swollen" disc – that may induce pain by irritating the outer anular fibers and thereby eliciting a pain response. The influx of fluids increases the intradiscal pressure and may result in internal derangement of the disc, particularly rupture of anular fibers. (22,23) It is not stated how the fluids enter the disc, i.e., whether through the periphery of the disc or the endplates or both. Proteoglycan solutions in varying concentrations regulate the degree of resistance to fluid flow and the transport of solutes. (32) There may be a derangement of this proteoglycan solutions and the matrix which allows swelling to occur. This rapid swelling of the nucleus pulposus is thought to precipitate biochemical changes which can lead to disc degeneration. (23) If true, this would help to explain the mechanism causing the Gonstead "Stages of Disc Degeneration" with the acute, swollen Gonstead D1 disc representing a disc with fluid ingestion. In this scenario, quick restoration of function of the affected spinal functional unit would undoubtedly have a highly beneficial effect.

**Blockage of Transport System**

When diffusion into the disc is blocked or reduced, it is thought to be an indication for the process of disc degeneration. It is not known whether changes in the vascularity of the endplate is a cause of or a result of degenerative disc changes. (24)

Calcification is thought to reduce nutrient transport into the disc as it inhibits the passage of various molecules that would have difficulty passing through a calcified endplate. (15) It is not known whether endplate calcification leads to disc degeneration or vice versa. (9,24) It is not uncommon to find fibrous transformation. fissuring, and breakage of the cartilaginous endplate in the third decade with bony invasion in the fourth decade. (13) The subchondral bone of the vertebral body can develop osteophytes that project into the cartilaginous endplates that may affect nutrient transport. (25)

Scoliosis has been related to endplate calcification and disc degeneration. The level of the disc where nutrient transport was most impeded was at the apex of the curve. (9,26)

Various disorders affecting the blood supply to the vertebrae and discs may impair the vascular supply to the disc, and thereby, lead to disc degeneration. (9) Endplate breakage, such as focal damage by Schmorl's nodes or large area damage by listhesis also has a significant effect on diffusion of nutrients. (3) Cinotti et al state that endplate injury leads to disc degeneration. (27) Atherosclerosis of the abdominal aorta and blood disorders may inhibit nutrient transport into the disc. (9)

Humoral regulation of blood flow to the endplate region has been found as Wallace el al found that infusion of acetylcholine increased endplate blood flow which shows the presence of muscarinic receptors in these vessels. (28) Therefore, there is neurologic control of nutrient transport via changes in blood flow. Sensory nerve fibers found in the endplate and vertebral body may cause pain generated from these structures in the presence of immunoreactive cells from chondrocytes, and this may result in an inflammatory response. (29) It is possible that this endplate inflammation may affect nutrient transport.

The effect of smoking on disc health is controversial. Studies have found a significant effect, not only on the circulatory system in general where it causes a reduction in solute exchange capacity, but also, a reduction in cellular uptake rate and the production of metabolites. (9,30) Both oxygen transport and lactic acid removal may be affected by constriction of microcirculation in smokers. (9,31) Uei et al found changes in gene expression in disc cells within two weeks of initiation of exposing rats to cigarette smoke. (32) Long-term use of nicotine has been found to cause changes to the capillary beds in the end plates. (6) Holms and Nachemson noted that some of the controversy of the possible effect of smoking on the disc may be due to the fact that most studies compare smoking to the subjective complaints of lower back pain rather than to structural or physiological changes. (31)

The importance of early action to re-establish more normal function the the spine, in particular, the disc is of utmost importance. The focus of the Gonstead adjustment on re-establishing improved disc and spinal function is important in spinal health. It would behoove the Gonstead chiropractors to research the effect of good segmental selection and line-of-drive to improve the injured disc. It might be possible to more quickly and effectively improve an injured disc and spine.

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VB = vertebral body / AF = anulus fibrosus / NP = nucleus pulposus /
VS = vein system / CT = capillary terminals / CEP = cartilaginous endplate /
SF = Sharpey's fibers