TRANSFORMATION

Dr. M's SCIENCE NOTES

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Mission Statement: Transformation uses every available resource to stay on the leading edge of clinical nutritional science by providing the health care community with the highest quality products, protocol, and research. The services that Transformation provides to the practitioner are better than and cost less than those that the practitioner could otherwise obtain.

CELLULAR INJURY, part 1:
The Dynamics of Cellular Homeostasis and Inflammation

The body's wellness requirement is based on cellular structural and functional integrity. The genes, their expression, the regulation of their expression, and the various interactions of these genes with nutrients and other molecules (endogenous and exogenous) determine this cellular integrity. Other factors include the cellular neighborhood of the cells, the availability and qualitative nature of the nutrients, and the level of activity of the cells. The multitude of factors that affects the integrity of the cell creates a constant challenge. At any time, the cells are likely to be disrupted from their balanced state. That balanced state is called homeostasis. In order to maintain wellness and health, the various cells need to be in balance within their environment and optimally perform their biochemical reactions.

The cells are under a constant challenge. As a result, they maintain a dynamic process of keeping their homeostasis. They do this by either adaptation to or the removal of the intervening factor. In other terms, it could be said that cells are constantly subjected to injurious factors. Injury is defined here as any process that results in disrupting cellular homeostasis.

The various injurious agents that affect cellular homeostasis include:

- structural damage such as burst blood vessels and torn muscles
- overuse of some tissues or organs such as in exercise
- lack of adequate concentration and/or supply of oxygen
- inadequate concentration of some molecules in the body such as high or low glucose, salts, potassium
- inadequate secretion of various hormones, neurotransmitters, and other molecules
- accumulated waste materials in the various compartments of the body
- biological agents such as virus, bacteria, endogenous altered molecules
- chemical agents such as pesticides, cosmetics, herbicides, food additives
- radiation and UV exposure

Despite the constant burden of these injurious agents, the cells try to adapt in order to survive. There are various adaptation methods that the cells use. The main adaptation strategies include:

- atrophy
- hypertrophy
- hyperplasia
- metaplasia
- accumulation of deposits within the cells
- irregularities in cell regeneration
- gene expression

As the cells adapt, they could go on and readjust to a new level of balance and homeostasis. However, that adaptation often undermines the cells long-term ability to adjust to further challenges. Additionally, as the challenging and injurious factors become persistent or recurring, the cells lose their ability to adapt and/or repair any damages, and thus initiate a deterioration process that may be irreversible.

Most cellular injuries include some form of ischemia or hypoxia. Hypoxia refers to low oxygen supply and usually involves glycolysis but with reduced Krebs cycle and oxidative phosphorylation. As hypoxia progresses, the cell will lose its vitality and degeneration sets in unless the condition is repaired to renew adequate oxygen supply.

Ischemia refers to the loss of blood supply to the tissues, which results in a lack of oxygen and nutrients. As ischemia continues, there will be complete loss of cellular functionality, depending on the severity of the injury and the nature of tissues affected. There is a point during the ischemic event where the damage is irreversible called point of no return. At this point, the cells cannot be salvaged. Ischemia is more damaging to the cells than hypoxia.

Either as a result of hypoxia or ischemia, lack of oxygen decreases ATP production. Furthermore, lack of ATP production either by inadequate oxygen supply or mitochondrial damage will result in the following biochemical impairments:

- increased glycolytic reactions
- depletion of glycogen reserves
- loss of various vital molecules (proteins, lipids, DNA, RNA, enzymes, coenzymes)
- reduced activity of sodium pump ATPase
- increased loss of intracellular potassium
- increased salt inside the cells
- increased water inside the cells, leading to swelling and extension of the cellular structures
- swelling of the mitochondria
- swelling of lysosomes and leak of lysosomal enzymes, resulting in hydrolysis of cell content
- deposits in the mitochondria
- extensive damage to cell membranes
- disruption of protein synthesis processes due to lack of energy and structural damage
- increased concentration of lactic acid, inorganic phosphates, and purines in cell
- leak of cell contents into extracellular spaces
- reaction with calcium forming calcium soaps

It should be noted that these injuries often occur in the body, albeit at much lower rates, and are readily repaired. However, as mentioned above, the ability of the cells to repair those constant injurious damages to which they are subjected is closely related to their access to vital nutrients that need to be readily provided via food selection, digestion, absorption, metabolism, and the elimination of wastes.

It is often assumed that injuries that are neither seen nor painfully felt are non-existent. This may be a bad assumption. The body is continuously bombarded with internal and external factors that tend to disrupt its homeostasis. There is therefore a constant shift between equilibrium (homeostasis) and disequilibrium (the risk of disease or pathology) within

the tissues. Every effort should therefore be made to constantly place the body only in the best conditions that enhance the prevention of injury and facilitate reparation when damage does occur.

Some of the damages listed above are exploited as diagnostic tools. As a result of cell leak, cell contents are often used as a diagnostic tool. For instance, testing for liver tissue integrity via the determination of liver enzymes in the blood is a good example. Under normal conditions, some of the liver enzymes should not be found above certain baseline levels within the general blood circulation. However, when those enzymes are present in higher levels, it is an indication that some of the hepatocytes are lysed and that their contents have leaked into general blood circulation.

Besides oxygen, another common factor in cellular injury is increased intracellular calcium levels. As the cell membrane loses its integrity, often as a result of damage in the cellular active transport mechanism, calcium infiltration inside of the cell is increased. This increase in intracellular calcium leads to further disruption of cellular structures as well as increased degradation of various molecules such as lipids, proteins, and nucleic acids. Additionally, the high levels of calcium inside of the cell will increase the use and degradation of ATP, which is already in low supply (as described above), culminating in the various injuries that the cell is undergoing.

The membrane structure is very critical to the mitochondrial function in producing ATP. Initial damage to the plasma membrane, for instance (as mentioned above), may lead to further membrane damage. As the cell membrane loses its integrity, there is no controlled separation between the inside and the outside cellular environment. Furthermore, the structural disintegration of the cell membrane will lead to disruption of other structures including mitochondrial, lysosomal, and nuclear membranes depending on the severity of the initial damage and the cell's ability to repair the damage. Should the cell fail to correct the damage in a timely manner, there is inflammation and/or degeneration.

Thus, cellular damage, including mitochondrial membrane damage, impairs oxygen utilization and reduces net ATP production. As oxygen is not used properly in the oxidative phosphorylation pathway to produce ATP, excess oxygen could act as free radicals, which will oxidize lipids, nucleic acids, and other molecules. This will lead to a cascade of free radical damage.

Inflammation, in general terms, may be defined as the body's response to an imbalanced (injurious) state and its return to homeostasis. As a result of any injury, the cells respond by initiating an inflammatory process. This is especially the case as the cells undergo deterioration. The intensity and duration of the stages in the inflammatory process may vary with the causative agents. There are various steps in the inflammatory process. The steps include:

- signal of a disruption in cellular structural and/or functional integrity
- setting up a defense mechanism against further damage
- initiating a process leading to reparation of the cellular structural and/or functional disorders

This set of dynamics (from injury to adaptation to deterioration) occurs readily. However, the rate of its occurrence varies from person to person. The extent of variation depends on genetic predispositions, nutrient acquisition, environmental factors, and an ability to manage various stress factors.

It should be noted that injuries occur to everyone and at different rates. Most cell injuries lead to the following characteristics:

- reduced or lack of oxygen supply
- reduction in energy output
- reduction in protein synthesis

- membrane damage and loss of selective permeability
- increased free radical damage

In order to maintain an optimum injury repair system within the body, it is important to maintain a good nutrient acquisition system (see *Dr M's Science Notes, v1* - "Nutrient Acquisition: The Foundation of Wellness"). In addition, one of the major benefits of supplemental oral proteolytic enzymes is to increase blood flow, thus improving oxygen supply, reducing acidity in tissues and helping delivery of nutrients to tissues (see *Dr M's Science Notes, v3* - "Proteolytic Enzymes: Applications and Benefits").