Image Awareness Wellness Institute

The Cell Part 3: Energy Crisis!

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Introduction

Access to energy is the foundation of any healthy city. Without energy nothing happens. The same is true of the cell. The capacity to produce abundant energy is a characteristic of every healthy cell. Energy deficit is an identifying characteristic of any sick or diseased cell. The cell produces energy in a special power plant called the mitochondrion. Every cell has many mitochondria, the greater the energy requirement the greater the number of these important structures within the cells.

Mitochondria are totally inherited from one's mother. This is because the mother's egg contains mitochondria but sperm do not.

Cells have from one to thousands of mitochondria. Liver cells have 1,000 to 2,000 mitochondria which take up one fifth of the volume of the cell. The heart and muscle cells also have large numbers of mitochondria which increase in number and efficiency in response to exercise.

The mitochondria have an inner and an outer membrane. The outer membrane allows small molecules to freely pass. The inner membrane is largely impermeable unless special transport molecules are used. The inner membrane contains large quantities of proteins which play a key role in energy production. The inner membrane contains an unusual phospholipid, cardiolipin, which helps make the inner membrane impermeable.

The surface area of the inner membrane is about five times as great as the outer membrane due to special structures called cristae. The following page contains an image of cristae captured from a liver mitochondrion of a rat. (Work done at the Wadsworth Center's Resource for Visualization of Biological Complexity.) Cristae are tubular projections connected to each other and to the inner membrane.

The capacity to produce abundant energy is a characteristic of every healthy cell.

Cells that have a greater demand for energy have mitochondria with greater numbers of cristae. The cristae increase the surface area where energy producing reactions can take place. The space within the inner membrane is called the matrix.

The mitochondria utilize about 85% of the oxygen consumed by the cell to generate ATP. Due to this high oxygen consumption, the mitochondria are an important source of internally generated free radical oxygen species which can potentially damage not only the mitochondria, but also other parts of the cell.

Two classes of nutrients assume great importance in the functioning of the mitochondria. The first is the vitamins and minerals essential for the generation of energy. The second is a sufficient antioxidant supply to curtail potential free radical damage in the process of this energy production.

Perhaps an illustration can clarify this. Think of the energy production of the mitochondria as a fire in a fireplace. The fuel would be the carbohydrates, proteins and fats we consume. The fire itself would incorporate the vitamins and minerals involved in the production of energy.

A fire emits sparks which can start a fire in the home. This is why a fireplace has a screen to contain the sparks. The screen mops up sparks just as antioxidants inactivate free radicals generated in the process of energy production in the mitochondria.

Reference:

Chew, Boon P., and Park, Jean Soon, Carotenoid action on the immune response, *J. Nutr*., January 1, 2004; 134(1):2575-2615.

https://commons.wikimedia.org/wiki/File:MitochondrionCAM.jpg

Energy Plus

The role the mitochondria play in cellular health goes far beyond that of energy production. Mitochondria also play a key role in cellular communication or signaling.

As cells develop they take on the characteristics of the tissues to which they belong. Thus we have cells in the liver, lung, and muscle. Each of these cells has unique characteristics. The development of cells into specific tissue types is called cellular differentiation.

Cellular differentiation requires healthy mitochondria. Loss of cellular differentiation is a characteristic of cancer. The weaker the process of differentiation, the more aggresive a cancer tends to be.

Another important cellular process is apoptosis or cell suicide. Cells normally commit suicide when they become damaged to the point where they can no longer function properly. Mitochondria are involved in the process of apoptosis.

Mitochondria also play a role in cell growth and cell division. Cell division is particularly demanding on the nutritional resources available. The cell must first accumulate sufficient structural materials in the form of lipids and amino acids to produce a new cell for division before replication can take place.

Cell replication is particularly frequent among the cells which line the digestive tract and the immune cells when the body is under attack by invaders. Thus digestive problems or immune compromise can result from mitochondrial dysfunction or inadequate intake of the nutrients necessary for cellular replication..

Mitochondrial DNA

The mitochondria contain DNA just like the nucleus of the cell. Damage to this DNA damages the functioning of the mitochondria. Mutation of the mitochondrial DNA takes place at a much higher rate than damage to chromosomal DNA. Not only is damage to mitochondria more extensive than damage to chromosomal DNA, but the damage also persists longer.

Exercise enhances not only production of more mitochondria, but it also activates repair mechanisms for mitochondria and improves their health.

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Yakes, F. Michael, and VanHouten, Bennett, Mitochondrial DNA damage is more extensive and persists longer than nuclear DNA damage in human cells following oxidative stress, *PNAS,* January 21, 1997; 94(2): 514-519.

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B Vitamins

The energy produced by the mitochondria is stored as ATP. The set of reactions necessary to produce the energy is called the citric acid cycle or the Krebs Cycle many of us became familiar with in high school biology class.

The entire vitamin B complex is essential for the mitochondria to produce energy. In addition, the B complex factors prevent mitochondrial toxicity. The B complex factors which play an important role include B1, B2, B3, B5, B6, B7 or biotin, folate and B12.

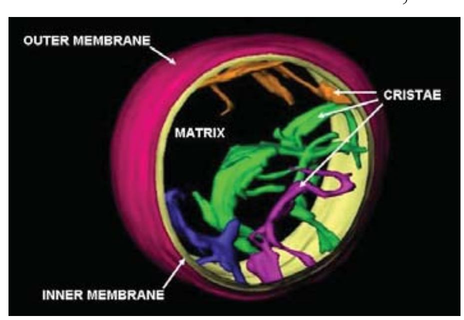
Thiamine or vitamin B1 is critical for energy production in the mitochondria. Carbohydrate conversion to energy is almost impossible without thiamine.

Deficiency is associated with brain damage in alcoholics (Wernicke's encephalopathy). The lack of thiamine allows glutamate to accumulate in the brain. Excessive levels of glutamate can kill brain cells. Deficiency of thiamine is associated with beriberi which is characterized by severe nerve damage.

Rats deprived of riboflavin or vitamin B2 rapidly lost the ability to burn fat to produce energy. A key enzyme in fat utilization was reduced by 35% within one day and by 75% after 28 days. Riboflavin's ability to increase mitochondrial energy efficiency has led to the suggestion that it be used as a prophylactic to prevent migraine. Deficiency can lead to easy fatigability and intolerance to exercise.

A recent paper by Sheila Seybolt suggests reassessing the use of alpha lipoic acid and niacinamide (B3) in therapy for schizophrenia. The combination of nutrients not only improves mitochondrial function, but also increases glutathione levels which reduces risk of mitochondrial dysfunction and oxidative damage. Niacinamide treatment for schizophrenia was advocated and used successfully by Abram Hoffer, the father of orthomolecular psychiatry.

Pellagra, the deficiency disease associated with insufficient vitamin B3, is characterized by the four D's: dermatitis, diarrhea, dementia, and death. Marginal deficiencies of the nutrient can contribute to skin conditions, di-



gestive difficulty, and mental deterioration.

Vitamin B5 or pantothenic acid has been shown to protect the mitochondria from free radical oxygen damage by increasing antioxidant activity (glutathione). Pantothenic acid increases energy production which leads to increased antioxidant protection of the mitochondria.

Vitamin B6 plays a central role in the conversion of protein, fat and carbohydrate to energy in the mitochondria. Deficiency of the nutrient is common due to the many vitamin B6 antagonists in the diet and environment. Deficiency can lead to cracks at the corner of the mouth, a shiny tongue, and inflammatory skin conditions. Deficiency can also negatively impact the nerves leading to irritability, depression and confusion.

Vitamin B6 works with folic acid and vitamin B12 in preventing the accumulation of homocysteine in the circulatory system. This compound is associated with heart disease, partially due to its ability to severely damage mitochondria.

One research group concluded that homocysteine accumulation is a clear risk factor for damage to the mitochondria as follows: "In summary, these studies demonstrate that homocysteine alters mitochondrial gene expression, structure, and function. In addition, homocysteine and H2O2 (hydrogen peroxide) act synergistically to promote mitochondrial damage, possibly by increasing the susceptibility of cells to oxidative stress."

Biotin is involved in a number of important activities in the mitochondria including glucose utilization. The nutrient has been shown to benefit diabetics. Biotin is found in few foods (egg yolk, liver, and cheeses). It is normally synthesized by bacteria in the digestive tract, but use of antibiotics can dramatically alter biotin status. Insufficient biotin can result in loss of coordination, skin conditions, tremor, and seizures.

References:

Depeint, Flore, et al., Mitochondrial function and toxicity: Role of the B vitamin family on mitochondrial energy metabolism, *Chemico-Biological Interactions*, October 27, 2006; 163(1-2):94-112.

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Hoppel, Charles, et al., Riboflavin and rat hepatic cell structure and function, *The Journal of Biological Chemistry*, May 25, 1979; 254(10):4164-4170.

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Seybolt, Sheila E.J., Is it time to reassess alpha lipoic acid and niacinamide therapy in schizophrenia?, *Med Hypotheses* (2010), doi:10.1016/j.mehy.2010.07.034

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Austin, Richard C., et al., Homocysteine-dependent alterations in mitochondrial gene expression, function and structure: Homocysteine and H2O2 act synergistically to enhance mitochondrial damage, *The Journal of Biological Chemistry*, November 13, 1998; 273, 30808-30817.

Vitamin E & Carotenoids

High concentrations of vitamin E are found on the inner membrane of the mitochondria. Both vitamin E and internally synthesized coenzyme Q10 are essential for supporting the functions and integrity of mitochondria. Modest vitamin E supplementation enhanced CoQ10 levels in mice. Ibrahim and associates determined that in rodents vitamin E was a key determinant of CoQ10 status. Unfortunately, statin medications used to treat heart disease block the metabolic pathway involved in synthesis of CoQ10.

The carotenoids are even more important than vitamin E for preserving the health and functioning of the mitochondria. The carotenoid astaxanthin has been shown to protect the mitochondria of vitamin E-deficient rats. The researchers wrote, "The inhibitory effect of astaxanthin on mitochondrial lipid peroxidation is stronger than that of α-tocopherol.... This inhibitory effect of astaxanthin being 100 to 500 times stronger than that of vitamin E." Chew points out that other carotenoids such as lutein and β-carotene have an affinity for the mitochondria as well.

Reference:

Ibrahim, Wissam H., et al., Dietary coenzyme Q10 and vitamin E after the status of these compounds in rat tissues and mitochondria, J. Nutr., September 1, 2000; 130(9):2343-2348.

Kurashige, Michi, et al., Inhibition of oxidative injury of biological membranes by astaxanthin, *Physiol. Chem. Phys. & Med. NMR.*, 1990; 22:27-38.

Chew, Boon P., and Park, Jean Soon, Carotenoid action on the immune response, *J. Nutr*., January 1, 2004; 134(1):2575-2615.

Alcohol

Alcohol can do serious damage to the mitochondria. The effects are most dramatic in the liver where alcohol is detoxified. It is damage to the mitochondria which leads to the liver disease associated with excessive alcohol intake.

Reference:

Hoek JB, Cahill A, Pastorino JG, Alcohol and Mitochondria: A Dysfunctional Relationship, *Gastroenterology*, June 2002;122(7):2049-2063.

Diseases

Damage to the mitochondria tends to lead to damage to tissues with the highest energy requirements. Since the brain and nervous tissue have very high energy requirements, it should not be surprising that faulty functioning of the mitochondria can lead to

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degenerative conditions of the nerve and brain tissue. Mitochondrial dysfunction has been implicated in Parkinson's disease, Alzheimer's, ALS, and Huntington's disease.

Excess saturated fat in the diet or simply a deficiency of essential fatty acids has been suggested as one contributor to mitochondrial dysfunction in Parkinson's disease. Excess saturated fat may interfere with the incorporation of essential fatty acids in the mitochondrial membranes leading to a failure to function properly.

The heart requires enormous quantities of energy to function properly. Mitochondria play a critical role in protecting heart function and defects are associated with heart failure.

Age related deterioration of the functioning of the mitochondria has also been associated with the development of osteoarthritis.

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Blanco FJ, Lopez-Armada MJ, Maneiro E, Mitochondrial Dysfunction in Osteoarthritis, *Mitochondrion*, 2004;4:715-728.

Heart Photo: http://www.flickr.com/photos/denn/169846212/

Magnesium

Magnesium is probably the most important cofactor or substrate involved in energy metabolism. It is involved in literally hundreds of enzymatic reactions. Among the earliest signs of magnesium deficiency are fatigue, lethargy and weakness as energy production is compromised. Muscle tightness or cramping are common signs of magnesium deficiency.

Magnesium deficiency compromises the ability of rats to produce energy within the mitochondria within 4 days and achieves maximum inhibition within 8 days. This study also showed that thyroid hormone which increases the metabolic rate can compromise the functioning of the mitochondria of heart tissues. Magnesium supplementation prevented the damaging effects of thyroid hormone. This raises the possibility that low thyroid function might be contributed to by low magnesium status. The lowered thyroid function would protect the heart since the mitochondria would not have to work as hard to keep the heart beating.

Reference:

Vitale, J.J., et al., The effect of magnesium deficiency on oxydative phosphorylation, *Journal of Biological Chemistry*, 1957: 573-576.

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