Pre-Diabetes Metabolic Syndrome, Type 2 Diabetes and Mitochondrial Function

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Type 2 Diabetes develops from a pre-Diabetes condition called Metabolic Syndrome (MetSynd). MetSynd is present in over 22% of the adult U.S. population, and it is made up of several interrelated disturbances of sugar and lipid metabolism. The major risk factors for MetSynd are: abdominal obesity, high blood sugar, increased levels of low-density lipoproteins (LDL) and reduced levels of high-density lipoproteins (HDL), elevated blood pressure, resistance to insulin and the presence of inflammatory molecules in the blood [1, 2].

Insulin resistance is one of the initial signs in the development of MetSynd [3]. Insulin is secreted into the blood by the pancreas in response to increased blood sugar levels, it assists in sugar metabolism and is essential for our development, growth and maintenance of proper blood sugar levels. When the blood concentrations of insulin are insufficient to regulate the above processes, insulin resistance occurs. Insulin resistance is one of the primary events in the development of MetSynd, which can ultimately lead to type 2 Diabetes.
Defects in the capacity to metabolize certain lipid components called fatty acids as well as defects in sugar metabolism are thought to play an important role in insulin resistance and MetSynd [2, 3].

Mitochondrial Damage, Metabolic Syndrome and Type 2 Diabetes

An important event in the development of MetSynd and eventually type 2 Diabetes is damage to cellular organelles in each cell called mitochondria where energy production occurs [2, 3]. Various studies point to generalized mitochondrial dysfunction in MetSynd and type 2 Diabetes along with fatigue [2]. Mitochondrial dysfunction has also been linked to chronic insulin resistance. This causes gradual pancreatic and other organ dysfunction due to lipid-oxidation and changes in mitochondrial structure, resulting in an uncoupling of mitochondrial energy production and increased production of damaging Reactive Oxygen Species (ROS) [2, 3]. The production of ROS results in mitochondrial membrane oxidation and membrane damage, which in turn, results in loss of cellular energy production and eventually fatigue.

When mitochondria function properly, the amount of ROS produced is effectively neutralized by endogeneous antioxidants and antioxidant enzymes present inside our cells. In MetSynd, type 2 Diabetes and associated diseases, however, excess ROS is produced in our cells that cannot be neutralized, and this results in damage to mitochondrial and other cellular membranes and their components. In obese, insulin-resistant, pre-Diabetic people higher amounts of damaged lipids called fatty acids are present. Even before a diagnosis of MetSynd or type 2 Diabetes, the accumulation of oxidized fatty acids inside mitochondria can result in progressive damage to these energy-producing structures. This also occurs in many elderly and obese people where oxidized fatty acids accumulate in muscle mitochondria, and this is related to mitochondrial dysfunction, loss of energy production and fatigue [2, 3].

The Role of Mitochondria in Aging and Fatigue

Fatigue or lack of energy occurs naturally during aging and is a common condition in many clinical diagnoses, including MetSynd, type 2 Diabetes, cardiovascular diseases, respiratory, musculoskeletal

and bowel conditions as well as infections and cancer [2]. Fatigue is related to reductions in the efficiency of mitochondrial energy production, and oxidative damage to mitochondrial components can impair energy production and cause fatigue in all of these conditions.

Mitochondria are also critical elements in the process of aging, and they have been proposed to be one of the regulators of aging and cell death. During aging and fatigue antioxidant enzymes, low molecular weight antioxidants and enzyme repair mechanisms cannot restore or replace enough of the ROS-damaged molecules to maintain mitochondrial function. Disease and infection can also result in excess oxidative damage that exceeds the abilities of cells to repair and replace damaged molecules.

Replacement of Damaged Mitochondrial Membrane Components by Lipid Replacement Therapy

Lipid Replacement Therapy (LRT) plus antioxidants, such as found in NT Factor®, has been used to reverse cellular oxidative damage and increase mitochondrial function in clinical disorders involving loss of mitochondrial function [5]. LRT is useful for MetSynd and type 2 Diabetes patients, because it replaces damaged lipids with undamaged lipids to ensure proper structure and function of cellular and mitochondrial membranes. In addition, it is combined with antioxidants, vitamins and minerals (such as in Propax with NT Factor® or Revacel with NT Factor®) to provide additional antioxidant protection. LRT plus antioxidants has proven to be an effective method to prevent ROS-associated damage to mitochondrial function. As discussed above, antioxidants alone may not completely eliminate or reverse ROS damage, and this is why LRT is an important addition to dietary antioxidant supplementation [2, 5, 6]. NT Factor's encapsulated lipids are protected from oxidation in the gut and can be absorbed and transported into tissues without significant oxidative damage [5].

In clinical studies LRT has been used to reduce fatigue and protect mitochondrial membranes. Products containing NT Factor® have been used in severely chronic fatigued patients, and it was found to reduce their fatigue approximately 40% within 8 weeks [6]. In four clinical trials NT Factor® in moderately and severely fatigued subjects was found to result in increased mitochondrial function and improved fatigue scores. For example, in patients with chronic fatigue there was a 35.5% reduction in fatigue with a proportionate increase in mitochondrial function. The results indicated that in moderately to severely fatigued subjects dietary LRT plus antioxidants can significantly improve and even restore mitochondrial function and significantly improve fatigue. Similar findings with LRT and antioxidants have been observed in Chronic Fatigue Syndrome and Fibromyalgia Syndrome patients [6]. The advantage of LRT plus antioxidants over antioxidant mixtures alone is that further oxidative damage is reduced and damaged (oxidized) lipid components are gradually replaced, restoring function to cellular membranes and mitochondria.

Metabolic Syndrome, Atherosclerosis and Coronary Heart Disease

Atherosclerosis involves chronic inflammatory damage to blood vessels due to ROS oxidative damage, lipid accumulation, inflammatory response, vessel cell death and thrombosis (presence of blood clots), which can eventually result in the occlusion of heart and other organ blood vessels [2]. A main cause of cardiovascular diseases and stroke, atherosclerosis is characterized by a number of risk factors, including abnormalities in lipoprotein distribution, increases in blood inflammatory proteins, and changes in vascular endothelial cell adhesion molecules. In the cardiovascular system ROS plays an essential physiological role in maintaining vascular integrity, but when ROS are in excess, they play a pathological role in cardiovascular dysfunction.

The process of atherosclerosis is thought to begin with abnormalities in lipoprotein subclasses, their remnants, and low-density lipoproteins (LDL), all hallmarks of MetSynd. In MetSynd lipoproteins and their remnants are susceptible to oxidation, and the presence of the oxidized lipoprotein subclasses is significantly associated with an abundance of innate immune cells called macrophages in atherosclerotic lesions.

When they interact with the blood vessel wall, the oxidized lipoprotein subclasses can induce endothelial adhesion molecules, which attract macrophages. The adhesion and movement of adherent macrophages to subendothelial tissue layers and their differentiation into inflammatory, ROS-producing macrophages is highly associated with atherosclerotic plaques. These plaques can break off and form blood clots or thrombi that can occlude blood vessels in the heart, resulting in myocardial infarction, heart failure and stroke.

Thus the use of products containing NT Factor is an important dietary advance in helping prevent the most common diseases associated with aging.

References

1. Fonseca VA. The metabolic syndrome, hyperlipidemia and insulin resistance. Clin Cornerstone 2005; 7: 61-72.

2. Nicolson GL. Metabolic syndrome and mitochondrial function: molecular replacement and antioxidant supplements to prevent membrane oxidation and restore mitochondrial function. J Cell Biochem 2007; 100: 1352-1369.

3. Houston MC, Egan BM. The Metabolic Syndrome. Pathophysiology, diagnosis, clinical aspects, prevention and nonpharmacologic treatment: emphasis on lifestyle modifications, nutrition, nutritional

supplements, vitamins, minerals, antioxidants, weight management and exercise. J Am Nutraceutical Assoc 2005; 8(2): 3-83.

4. Huang H, Manton KG. The role of oxidative damage in mitochondria during aging: a review. Front Biosci 2004; 9: 1100-1117.

5. Nicolson GL. Lipid replacement as an adjunct to therapy for chronic fatigue, anti-aging and restoration of mitochondrial function. J Am Nutraceutical Assoc 2003; 6(3): 22-28.

6. Nicolson GL, Ellithrope R. Lipid replacement and antioxidant nutritional therapy for restoring mitochondrial function and reducing fatigue in chronic fatigue syndrome and other fatiguing illnesses. J Chronic Fatigue Syndr 2006; 13(1):5 7-68.

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