Cellular Nutrition for Vitality and Longevity

Every cell depends upon CoQ10 for energy production & antioxidant defense. A safe, effective therapy for heart disease, CoQ10 may help extend life span & protect against degenerative disease

Vitality means energy plus resistance to stress. Cells produce energy through a process called "cellular respiration." But oxidative stress caused by free radicals can damage the cell and inactivate cellular respiration. The cell therefore mobilizes an antioxidant defense system to protect itself against oxidative assault.

Nature in her economy created one molecule to serve both purposes. Bioenergetic fuel and master antioxidant, CoQ10 plays vital roles in both cellular respiration and antioxidant defense.

Nature devised a third vital role for CoQ10 in the bloodstream. Most CoQ10 is carried through the bloodstream by LDL, which also carries the "bad" form of cholesterol. CoQ10, along with vitamin E, helps prevent atherosclerosis by protecting LDL cholesterol from artery-clogging oxidation.

Heart, brain and muscle cells consume a great deal of energy. They are also easily damaged by free radicals. Thus it is not surprising that CoQ10 applications and research focus on these body systems. Moreover, aging is marked-many scientists would say caused-by oxidative damage and declining cellular energy production. Emerging research highlights the potential of CoQ10 as a general anti-aging therapy.

The body synthesizes CoQ10 and absorbs small amounts from food. In addition, CoQ10 has been available as a nutritional supplement since The Life Extension Foundation introduced it to the American public in 1983. Dozens of clinical trials demonstrate that oral CoQ10 supplements raise blood levels of CoQ10 safely with no significant side effects. As age increases, CoQ10 synthesis declines but CoQ10 supplements are better absorbed.

When we picture health and nutrition, few of us imagine the cell. But with a moment's reflection, it is obvious that health begins in the cell. A decline in the capacity of the cell to generate energy and respond to stress leads to disease and biological degeneration. Both of these capacities are bound up with the mitochondria, the "energy factories" of the cell.

There are hundreds of mitochondria in a typical cell. Each contains a unique form of DNA inherited from the mother alone. The main business of the mitochondria is cellular respiration, the primary energy source in the cell and in the body (see Figure 1). However recent research points to the mitochondria as the crucial targets of oxidative stress and as regulators of cell death.

Antioxidant defenses

The paradox of aerobic (oxygen dependent) life is that oxygen is toxic to biological molecules and cells. Oxygen, including the oxygen used in cellular respiration, tends to form free radicals in the body. These free radicals oxidize biological molecules, just as iron oxidizes when it rusts. The oxygen that cellular respiration transforms into energy must therefore be considered a hazardous substance in the body. Biochemists call this the "oxygen paradox."

Nature's resolution of this paradox is the antioxidant defense system. An antioxidant is a molecule that neutralizes free radicals in the same way that baking soda (sodium bicarbonate) neutralizes excess stomach acids. Every organism is endowed with a coordinated system of antioxidants, but this system is imperfect. Consequently, free radicals actively

damage the three main classes of biological macromolecules-lipids (fats), nucleic acids (DNA, RNA) and proteins.

Nature's second line of defense is a removal and repair system for damaged macromolecules, but this too is imperfect. Consequently, oxidative damage accumulates through life and increases in old age.

Oxidative stress is a relative term for an imbalance between the capacity of the body's antioxidant defense system and the level of free radicals-in short, an imbalance between antioxidants and pro-oxidants. Oxidative stress increases when antioxidant defenses weaken or free radical levels rise. It is now widely accepted that oxidative stress figures prominently in cell transformation and cancer, atherosclerosis and heart disease, both acute and chronic inflammatory conditions, cataracts, and neurodegenerative diseases such as Alzheimer's disease. We can decrease oxidative stress by bolstering the body's antioxidant defenses and reducing free radical generation or exposure.

Oxidative stress tends to escalate over time. When a cell or molecule is damaged by oxidative stress, it tends to malfunction so as to cause additional oxidative stress. Biochemists refer to such a downward spiral as a "catastrophic vicious cycle." Oxidative stress and bioenergetic deficiency are locked together in just such a vicious cycle. The downward spiral of increasing oxidative damage and dwindling cellular energy production is a hallmark of aging and many degenerative diseases.

In 1956, Prof. Denham Harman proposed the now-famous "free radical theory of aging." The theory holds that as we age and the oxidative damage the body has sustained over the years takes its toll, the level of oxidative stress itself rises. This may be compared to a rusting, crumbling building that is subjected to ever harsher rain and wind. The cumulative effect over time of this buildup of oxidative damage is aging, degeneration and death. In 1972 Harman, with his usual prescience, singled out the mitochondria as key targets of oxidative stress. Jaime Miquel took up this idea in a 1980 study that initiated modern research on mitochondrial aging, a subject we return to in the next installment of this article which will appear in an upcoming issue of the magazine.

Master antioxidant

The Janus faces of oxygen- sustainer and destroyer of life-are both bound up with CoQ10. CoQ10 facilitates the production of energy from oxygen, while protecting the organism from the "dark side" of oxygen. Nature created a biomolecular complement to oxygen in CoQ10, which may be regarded as equally fundamental to aerobic life.

The greatest biohazard the body's antioxidant defense system must face is the oxidation of lipids (fats). This occurs in cell membranes, the brain (over 50% fatty acids), and blood lipoproteins (which carry cholesterol). The oxidation of lipids, known as lipid peroxidation, is a chain reaction that damages the biological molecules in its path and generates toxic byproducts.

The fat-soluble antioxidants-primarily vitamin E and CoQ10-protect against lipid peroxidation. This preserves the integrity of cell membranes and protects DNA, proteins and blood lipids from oxidative damage.

Why does a source of cellular energy such as CoQ10 double as an antioxidant? Cellular respiration takes place in a lipid-rich membrane inside the mitochondria, and is itself a source of oxidative stress. The cellular respiratory chain is thus highly vulnerable to lipid peroxidation. CoQ10 helps protect the integrity of this membrane while shielding the respiratory chain from free radicals. This, coupled with CoQ10's essential role in energy production, helps prevent the vicious cycle of bioenergetic decline and oxidative stress (see the sidebar "Breaking the Vicious Cycle").

Much of the damage done by lipid peroxidation is the work of long-lived toxic byproducts such as HNE and MDA. HNE (4-hydroxy-2-trans-nonenal) impairs cellular respiration and DNA synthesis, while MDA (malondialdehyde) is associated with the arterial plaque instability thought to cause heart attacks. A recent Polish study specifically shows that CoQ10 supplementation reduces total HNE and MDA. Industrial workers regularly exposed to organic solvents that cause lipid peroxidation showed significant reductions in the HNE plus MDA blood level after taking CoQ10 supplements for four

weeks.

We have reviewed forty years of research on CoQ10's well-known roles in cellular energetics, antioxidant defense and cardiovascular therapy. The next installment of this article will take a look forward into the frontiers opened up by recent research on CoQ10 as a potential anti-aging therapy.

Cellular Energy Generation

Mitochondria are the power plants of the cell. They transform oxygen and nutrients into energy and water through a process called cellular respiration. The many finger-like folds in the mitochondrial inner membrane house respiratory chains (bottom panel) where energy is produced. CoQ10 (yellow) carries electrons across the chain while pumping protons (red) through the inner membrane (purple). The return flow of protons into the last component of the chain (blue) drives synthesis of ATP, the energy storage molecule.

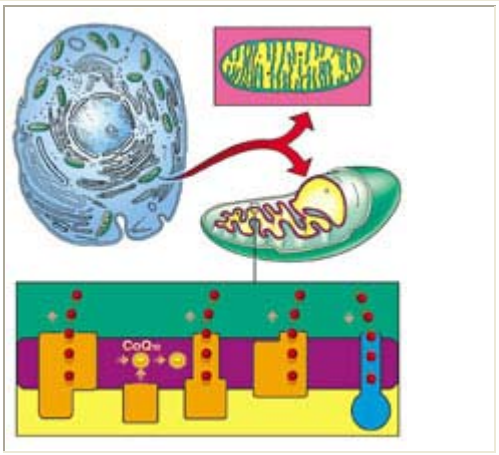

Figure 1. Structure of a cell (upper left), with detail of a mitochondrion (upper right). The cellular respiratory chain (bottom) generates energy.

Historical note: In 1961 Peter Mitchell proposed that the flow of electrons across the respiratory chain is coupled to the flow of protons through the inner membrane. According to his "Q cycle" model of the third component of the chain, CoQ10 couples electron flow to proton flow as it cycles through changes of state. The scientific community resisted Mitchell's unorthodox theory for many years, but in 1978 he was awarded the Nobel Prize in Chemistry for this work, and subsequent research has provided further vindication of his ideas. The pumping of protons from the first and fourth components of the chain is not yet understood, however there is evidence for a modified Q cycle in the first component. -

Breaking the vicious cycle

The vicious cycle of bioenergetic deficiency and oxidative stress depletes cellular vitality. Cells caught in this cycle produce little energy but a great deal of oxidative stress, and may eventually die. When a large enough proportion of the cells in a tissue or organ are lost or degraded in this way, it can no longer function adequately.

You might think that cellular respiration would be sheltered from oxidative stress, but this is not the case. Cellular energy production itself generates oxidative stress. In addition, it takes place in a lipid-rich membrane inside the mitochondria. Lipid peroxidation in this membrane damages the cellular respiratory chain. Damage to the respiratory chain not only impairs energy production but also further increases oxidative stress. This is because the damaged chain leaks electrons that tend to form free radicals, and also because an intact respiratory chain is required for the efficient recycling of CoQ10 and other antioxidants. In this way, oxidative damage and bioenergetic decline reinforce each other in a vicious cycle.

Antioxidants address only one side of this problem, while CoQ10's dual action addresses both sides. As an energy producer CoQ10 supports cellular respiration, while as an antioxidant it helps protect the respiratory chain from oxidative damage. Research by Prof. Lars Ernster's group at Stockholm University demonstrates that the CoQ10 contained in the inner mitochondrial membrane protects membrane lipids, proteins, and enzymes-including the components of the respiratory chain-from oxidation.

Hundreds of laboratory studies and clinical trials over the last thirty years have demonstrated the effectiveness of

CoQ10 in pathologies involving bioenergetic deficit and oxidative stress. An interesting example is male infertility, which can be caused by inadequate energy production in sperm leading to reduced motility, and by oxidative damage to sperm especially through lipid peroxidation. A recent pilot study found that CoQ10 supplementation more than doubled fertilization rates in male infertility patients.

References*

The website of the International Coenzyme Q10 Association contains an excellent "Introduction to Coenzyme Q10" by CoQ10 researcher Peter H. Langsjoen, MD (cited above as Langsjoen PH, 1994). See also the "Overview of the Use of CoQ10 in Cardiovascular Disease" for Dr. Langsjoen's expert review of the literature in this area (cited above as Langsjoen PH et al., nd). The Association's website can be found at wwwcsi.unian.it/coenzymeQ/indexd.html

A note on scientific terminology

Research papers may refer to Coenzyme Q10 as ubiquinone, coenzyme Q or ubidecarenone. Coenzyme Q10 in its antioxidant form is referred to as ubiquinol, ubiquinol-10 or CoQ10H2. The scientific name for Coenzyme Q10, ubiquinone, means "ubiquitous quinone" since it is found in every cell and belongs to the chemical family of quinones. Free radicals are more properly referred to as reactive oxygen species (ROS) and reactive nitrogen species (RNS).

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