Nestlé HealthScience

The Value of

cellular nutrients designed to restore cellular (mitochondrial and metabolic) processes that often decline with age

Evidence has emerged on both the changes in mitochondria that generally occur with age or the onset of medical conditions, and novel cellular nutrients able to act on these metabolic pathways important for energy and vitality, strength and stamina, and protection.

OFTEN WITH AGING, THERE IS A PERCEIVED NEED FOR MORE ENERGY, ENDURANCE, STRENGTH AND STAMINA

27% of adults aged **>50 years** report they had **too little energy** to do things they wanted to do in the last month, and 6% had weakness indicated by poor handgrip strength.[1]

Indeed, these **signs of fatigue and weakness** are among the most common issues identified in a **large observational study of adults age 50/55–64 years, of which 37% are pre-frail.**[2]

In a study to identify the specific outcomes important for older patients with **loss of muscle strength and function, fatigue** was the concern of most importance (for **27%**), followed by mobility (for **19%**).[3]

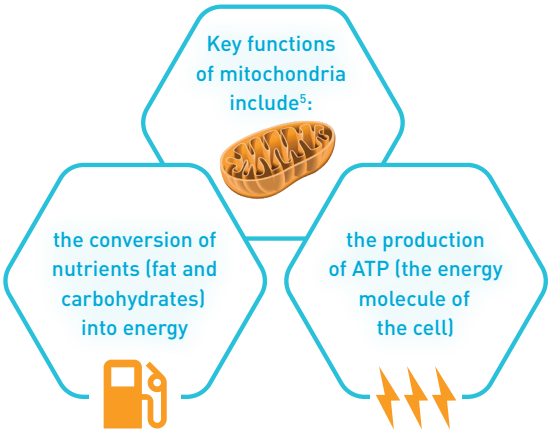
Among common chronic conditions, the **most frequent ailment is a state of impaired mobility,** prevalent in nearly **55%** of adults aged 50–70 years in the US.[4]

RESEARCHERS HAVE RECENTLY DISCOVERED MORE ABOUT THE BIOLOGY OF AGING AND THE IMPORTANT ROLE OF MITOCHONDRIA ON CELLULAR BIOENERGETICS AND MUSCLE FUNCTIONALITY

Mitochondria are organelles found in almost every cell which act to covert nutrients into energy (adenosine triphosphate [ATP]), supporting cellular bioenergetics in muscle and all organs throughout the body.[5–7]

Healthy mitochondria are especially vital for organs with a high demand for cellular energy, such as skeletal muscle, and the heart[8]; for example there are up to 5000 mitochondria per heart muscle cell.[9]

Importantly, mitochondrial dysfunction is common with older age or in disease conditions, and is one of The Hallmarks of Aging.[10]



These changes may impact energy and strength:

- With age, the capacity for ATP production often decreases by 8% per decade[5]
- With age beyond 50 years, skeletal muscle strength often declines by 1.5–5% per year[11]

Without taking special actions marked by baseline measures in observational studies, **the following changes in mitochondrial function can be detected (vs. younger adults) among older adults or those with conditions of accelerated aging:**

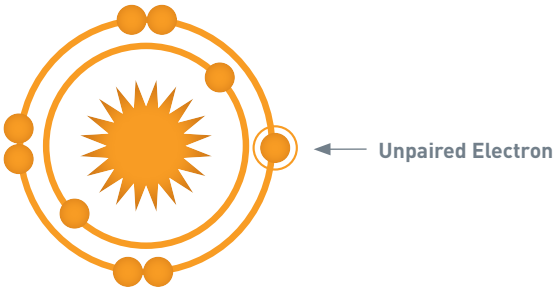
PROGRESSIVE SYMPTOMS OF MITOCHONDRIAL DYSFUNCTION[12,13]

Mitochondrial dysfunction has been indicated by:

- Limited mitochondrial production of ATP, the energy molecule of the cell, in older adults[5,8] and those with conditions of accelerated aging[15]
- Impaired mitochondrial fatty acid oxidation in older adults[7,16] and those with conditions of accelerated aging, such as HIV[17]
- Metabolic inflexibility in regulating mitochondrial oxidation of fatty acids and carbohydrates in an insulin-responsive manner in older adults[7] and those with conditions of accelerated aging, such as HIV[17]

SOME MARKERS OF AGE-ASSOCIATED CELLULAR DECLINE INCLUDE[5,7,10,12,14]:

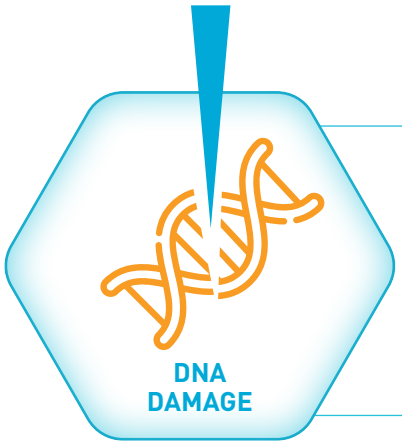
- GLUTATHIONE DEFICIENCY
- ELEVATED OXIDATIVE STRESS
- DNA DAMAGE
- A DECLINE IN MITOCHONDRIAL DNA
- MITOCHONDRIAL DYSFUNCTION
- DIMINISHED ENERGY PRODUCTION



Free radical

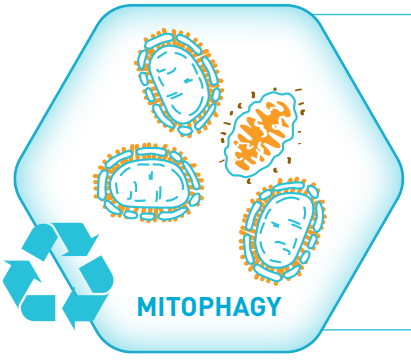
The Hallmarks of Aging

Adapted from: López-Otín C, et al. 2013.[10]

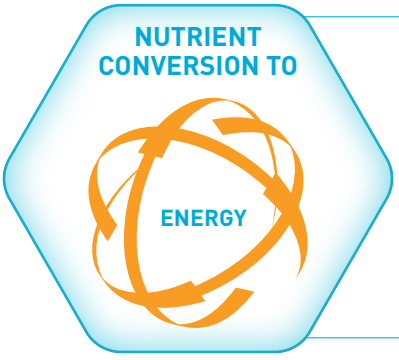


Contributors to mitochondrial dysfunction:

Cellular damage (DNA damage), caused by reactive oxygen species (ROS), often accumulates with older age or in disease conditions.[12] Reportedly, these are states of **glutathione deficiency, when the intracellular antioxidant and its precursor amino acids are at low concentrations, and cells are more susceptible to damage from oxidative stress.**[17,18]



The normal mitochondrial life cycle promotes continuous turnover, with mitochondria constantly being degraded (mitophagy) and replaced (biogenesis). However, the **ability to clear damaged mitochondria (mitophagy) is reduced** with age or in disease conditions.[6] In effect, damaged mitochondria can build up and contribute to mitochondrial dysfunction and diminish cellular bioenergetics in muscle and throughout the body.



With age or the onset of disease conditions **a decline is often observed in the coenzyme, nicotinamide adenine dinucleotide (NAD^+), which is essential to turn nutrients into energy and for normal mitochondrial metabolism.** While maintaining adequate levels of NAD^+ is necessary to support cellular homeostasis and energy production with age, results suggest that the concentration of NAD^+ declines up to 50% between ages 40 and 60 years.[12]

SPECIAL NUTRITIONAL INTERVENTION MAY TARGET CELLULAR (MITOCHONDRIAL AND METABOLIC) PROCESSES THAT OFTEN DECLINE WITH AGE, IMPORTANT FOR:

- **NATURAL PROTECTION[7,19]**
- **NORMAL METABOLISM (FUEL BURNING) AND ENERGY PRODUCTION[7,20]**
- **VITALITY AND IMMUNITY[18]**
- **STRENGTH AND STAMINA WITH AGE[21,22]**

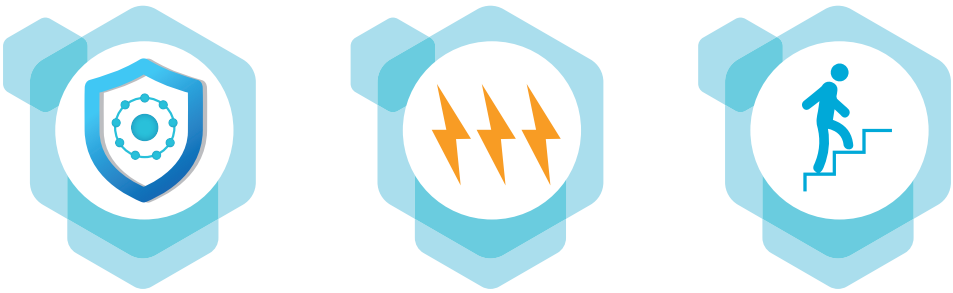
Aging research has evolved significantly in recent years. Researchers now know there is a time dependent decline of several cellular mechanisms that often starts in our 40s and accelerates in our 60s. This can be defined as 'Age Assoiciated Cellular Decline', and one of the key drivers behind the changes is mitochondrial dysfunction.[10]

For example, mitochondrial energy production is not as simple as providing fats and carbohydrates to the body, especially with age. Other 'cellular nutrients' are needed to support efficient energy metabolism.[7,20]

Beyond the classical essential and conditionally-essential nutrients, emerging evidence suggests other food components (e.g. phytochemicals) can lower the risk of major health problems.[23]

While each stage of the life cycle, including states of progressively older age, is known to have specific nutrient needs, conditions are more common in older age and can affect ingestion, absorption, metabolism, and excretion of conventional food sources and create distinctive nutritional needs.[24,25] Such conditions of accelerated aging may threaten to shorten life, yet risk factors can be modified to some extent by diet (nutrient intake), or by diet and exercise.[26]

Recent evidence has emerged on both the changes in cells and their organelles, mitochondria, that generally occur with age or the onset of medical conditions, and novel cellular nutrients able to act in a precise way within the cell on these mechanistic pathways important for cellular homeostasis and physiologic function.



Unlike classical macro- and micro-nutrients, this new class of cellular nutrients:

- May be available or derived from food sources, yet are likely to be consumed in inadequate amounts from a usual diet to cover cellular needs[14,27-29]
- Have been demonstrated to help restore natural cellular processes that often decline with age or in disease conditions[7,12,14,17,27]
- Work cell by cell, in all organs throughout the body; for example, to reduce mitochondrial dysfunction important for normal cellular bioenergetics[7,14,27]
- Specific nutrients are being examined for their regulation of gene expression or gene sets[22]

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