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# Helping Patients to Age Well

## *Applying the Free-Radical Hypothesis*

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**Chris D. Meletis, N.D.,  
and Ben Bramwell**

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**A**ccording to the U.S. Census Bureau, by 2030, 20 percent of the U.S. population will be over 65, compared to just 4 percent 100 years ago.<sup>1</sup> This means that we, as practitioners, shall be called upon increasingly to help our patients optimize their health as they get older. This can be achieved with careful and appropriate natural intervention. This includes not only encouraging patients to avoid common health problems such as heart disease, strokes, cancer, diabetes, and osteoporosis (see Table 1), but also showing patients how to strengthen their bodies' systems so that these people can enjoy their maximal life spans more fully. This article reviews some of the current understanding of aging and briefly discusses several strategies that may be useful in successfully managing health in aging patients. The research backs up our clinical observations that prevention is the key. We can teach patients that, in fact, the pursuit of a long and vibrant life is much like planning for a stable financial retirement, that the investments made along the way determine the style in which one enjoys much-awaited retirement years.

### **The Free-Radical Theory of Aging**

One of the most frequently discussed theories of aging is the free-radical theory of aging.<sup>2</sup> The basic idea of this theory is that a shift occurs between the amounts of pro-oxidants (which are needed for tasks

such as immune defense and cell communication) and antioxidants (which keep the pro-oxidants from doing too much damage to the human body). This shift leads to increased oxidative stress, less well-controlled cell functioning, and aging. The theory is based primarily on three observations: (1) free radicals are extremely reactive; (2) they are constantly being produced from oxygen in the body; and (3) natural defense systems exist to control the unwanted effects of free radicals.<sup>3</sup>

As the body processes food and captures its energy potential, storing this energy in the adenosine triphosphate molecule via the mitochondria, free-radicals are generated, specifically the superoxide anion O<sub>2</sub><sup>-</sup>, which damages the mitochondrial structure,<sup>4</sup> genetic material, and cell membranes throughout the digestive, endocrine, immune, circulatory, and nervous systems. Thus, it is clear that preventing free-radical damage is a critical part of enhancing and strengthening these body systems.

### **Support of the Antioxidant Scavenging Enzymes**

The body's defenses against free-radical activity include both antioxidant scavenging enzymes and free antioxidants such as vitamin C and Vitamin E. The enzyme systems are in the cytosol of the cell and in the mitochondria. These enzymes work together to change the superoxide anion to hydrogen peroxide and then to water or water and oxygen. The enzyme involved in the first step of the process, superoxide dismutase, requires zinc for its action.<sup>5</sup> One of the two forms of an enzyme required for the

second part of the process, glutathione peroxidase, requires selenium and reduced glutathione.<sup>6</sup> Good fueling with regard to biochemical cofactors along the steps of the biologic pathway is needed so that the process is not stalled. This is also vital between the first and second parts of the process because hydrogen peroxide can react additionally with metals, such as iron, to create the very reactive hydroxyl radical. Thus, it is essential to ensure that patients consume adequate levels of zinc, selenium, and reduced glutathione.

### **Possible Benefit of Antioxidant Supplementation**

Other antioxidant supports also include vitamin E and coenzyme Q10 (CoQ10), which quench free radicals directly, and oils, such as olive oil, which reduce the targets of free-radical damage in cell membranes. In one study that examined the long-term effects of antioxidant supplementation in mice, supplementation did not prolong lifespan per se, but it did result in significantly lower lung viral levels following a challenge with influenza virus.<sup>7</sup> Vitamin E also modulates the interaction between immune-system cells and the epithelial cells that line blood-vessel walls,<sup>8</sup> and this action may well account for the cardiovascular benefit of vitamin E supplementation. Recent research suggests that vitamin E's prevention of low-density lipoprotein oxidation is clearly dose-dependent, with 1200 international units (IU) per day offering significantly more protection than 400 IU per day.<sup>9</sup> In a preliminary study that examined the effects of supplementa-

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**Table 1: Prevention Strategies for Overcoming Common Health Problems in Aging Patients**

<b>Problem</b>	<b>Tell your patients</b>
Heart disease	Increase consumption of dark purple and red, bioflavonoid-rich fruits and vegetables. These help to prevent damage to blood-vessel linings by increasing vitamin E intake and antioxidant protection.
Cerebrovascular accidents	Maintain adequate thinness of blood by consuming foods such as garlic and cold-water fish on a regular basis
Diabetes	Ensure adequate intake of minerals, whole grains; avoid over-consumption of carbohydrates with too little protein or fiber; take chromium supplements.
Osteoarthritis	Consider supplementation with products that support healthy joint tissue, such as glucosamine sulfate
Cancers	Encourage sufficient detoxification by eating fruits and vegetables that are rich in phytochemicals such as limonene, sulforaphane, and dietary indoles that stimulate the liver's and intestinal tract's detoxification pathways. Men should consider increasing lycopene to support prostate health and women should consider increasing their isoflavone intake. This prevents genetic damage by supporting antioxidant pathways.
Lung infections	Increase water consumption to maintain moisture and integrity of mucous membranes; quit smoking and avoid second-hand smoke, and environmental irritants, such as dust and chemical fumes.

tion with CoQ10 and virgin olive oil, researchers found that both substances protect mitochondrial membranes from free-radical damage.<sup>10</sup> It appears that, while CoQ10 successfully scavenges free radicals directly, the addition of virgin olive oil prevents damage by increasing cell-membrane concentration of monounsaturated fatty acids, which are not as prone to free-radical damage as fatty acids with many unsaturated bonds.

Additional motivation for your patients to increase their consumption of monounsaturated fatty acids is provided by the results of a recent case-control study of 317 patients with prostate cancer and 480 controls. The study found that participants who reported the highest consumption of monounsaturated fatty acids cut their relative risk of prostate cancer by half.<sup>11</sup> These diets were high in vegetables, lycopene, vitamin E, selenium, and omega-3-fatty-acid fish oils. An addition-

al consideration in men's risk of prostate cancer is a recent study that examined the risk of prostate cancer and alcohol consumption and found that men who drank more than 96 g of alcohol per week had a threefold increased risk of contracting the disease.<sup>12</sup> Moreover, the same research showed an increased relative risk for obese men.

Other antioxidants that may be important in helping patients to achieve the maximum lifespan are carotenoids. In one study that examined levels of total carotenoids (carotenes plus xanthophylls), there was a positive correlation between carotenoid levels in serum and the brain and the maximum lifespans of eight mammal species, including humans.<sup>13</sup> The correlation did not exist, however, for retinol. While this work did not show cause and effect between longevity and total carotenoid level, it did reveal a trend that held up across several mammalian species.

### Vision Support

In addition, the carotenoid xanthophylls, lutein and zeaxanthin, may have an important role in eye health as humans age.<sup>14</sup> The retina is very susceptible to free-radical damage because of its high oxygen consumption, high amount of polyunsaturated fatty acids, and exposure to visible light.<sup>15</sup> And, while lutein supplementation is not probably a "magic bullet" for preventing free-radical damage in aging eyes completely, a cohort study of 1354 people found that persons in the highest quintile of lutein intake

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were only half as likely to develop cataracts as those who persons in the lowest quintile of lutein consumption.<sup>16</sup>

### Potential Benefits for the Brain and Spinal Cord

The benefits of adequate antioxidants may also extend to limiting age-associated decline in the nervous system. In recent research,<sup>17</sup> aging rats who had diets supplemented with antioxidant rich foods, such as spinach, strawberries, or blueberries, experienced reverses in age-induced declines in part of their cerebellums. The practical result was that the rats improved their ability to learn new motor tasks. If similar, antioxidant-rich interventions can help aging humans learn new motor tasks also, then antioxidant therapy would prove to be valuable in improving rehabilitation after traumas, such as strokes and spinal-cord injuries.

### The Importance of Glutathione

One substance which is starting to emerge as an important factor in healthy aging is glutathione. In addition to being a widespread antioxidant, glutathione is also needed to bind pollutants (xenobiotics) up and to keep the membranes of oxygen-carrying red blood cells stable.<sup>18,19</sup> Two studies on glutathione and aging in humans are worth serious consideration.

In the first study, which involved 169 healthy subjects, blood glutathione levels had decreased significantly (17 percent) in the 60–79 age group versus the 20–39-

Nutrient	Adult Dosage Range	Rationale
Zinc	15–30 mg/day	Needed for antioxidant enzymes
Selenium	200 µg/day	Needed for antioxidant enzymes
Vitamin C	500–1000 mg/day	Water soluble antioxidant
Vitamin E	400–1200 IU/day	Fat-soluble antioxidant; protects endothelial cells lining blood vessels
Coenzyme Q10	30–150 mg/day	Fat-soluble antioxidant, protects heart mitochondria
Virgin olive oil	As needed for food preparation	Increases the concentration of monounsaturated fatty acids in cell membranes and decrease free-radical targets
N-acetylcysteine	500–1500 mg/day	Supports production of glutathione
Carotenes <sup>a</sup>	25,000–300,000 IU/day	Increased tissue and blood levels correlate with increased lifespan across several mammal species

<sup>a</sup>Current research evidence suggests that supplemental carotene should not be given to patients who smoke.  
IU = international units.

year-old group. An interesting finding of this study was that the percentage of subjects with low glutathione in the oldest age group, people ages 80–99, was less (6 of 25 patients low in glutathione) than the percentage of subjects with low glutathione in the 60–79 age group (28 of 60 patients low in glutathione). One explanation for these results is that more of the low-glutathione patients died before age 80. It is also interesting that all of the subjects 80 years and older had glutathione levels higher than 400µg/1010 erythrocytes, suggesting that this level might be a survival limit.<sup>20</sup>

The second glutathione study sought a correlation between blood glutathione levels and the occurrence of conditions such as arthritis, glaucoma, asthma, emphysema, heart disease, diabetes, and others, which were lumped into a morbidity index. The results of the study showed that, while other factors, such as repressed anger, also correlate with higher morbidity, the strongest correlation factor, by far, was with low blood glutathione levels. Because the study had a small sample size (only 33), the study authors pointed out that larger studies should be done.<sup>21</sup>

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### Hormone Replacement

In the last 5 years, there has been an increased familiarity with the hormones melatonin and dehydroepiandrosterone (DHEA), which some scientists hoped might be the "fountain of youth." While such claims surely fall short of reality, there may be a legitimate place for the use of these hormones for aging patients.

Melatonin, for example, is ideal as a potent scavenger of the hydroxyl radical, because of melatonin's ability to move across fatty tissues with ease.<sup>22</sup> Because the hydroxyl radical may actually be the most damaging free radical made,<sup>23</sup> and given the human tendency toward lower melatonin production from the pineal gland as the body ages, it might be reasonable to encourage aging patients to take small amounts of melatonin to improve their antioxidant potential. Given that amounts as low as 300 µg are able to induce normal physiological levels in young adults,<sup>23</sup> the lowest available commercial dose of 500 µg seems to be reasonable.

DHEA, as mentioned above, has generated a flurry of interest—and controversy. Some concern would seem to be warranted, especially because DHEA can be converted to the other very powerful hormones, estradiol and testosterone (perhaps increasing the risk of patients developing hormone-sensitive tumors, as occurs in breast and prostate cancer). In a recent study, 280 healthy subjects between the ages of 60 and 79 were given either placebo or 50 mg of DHEA per day for 1 year.<sup>24</sup> During the study, the effects of supplementation on bone turnover, skin status, and libido were assessed. The researchers also examined changes in the subjects' amounts of

testosterone and estrogen. Observed benefits in bone turnover and improved libido were seen in some women over 70. Some benefit was also seen in skin status, more especially in women, with respect to the hydration of skin, epidermal thickness, sebum production, and pigmentation. All women in the treatment group had significant increases of estradiol versus the placebo group. Women older than 70 also had significant increases in testosterone. None of the increases in steroid levels raised levels above those found in younger adults. Men did not have significant increases of testosterone or estradiol compared to the placebo group by the end of the study. So, while the clinical improvements are good news for women, particularly those older 70, this route of supplementation may not hold as much promise for men and younger women.

### Maintaining Adequate Absorption

Another important aspect of aging well is maintaining adequate absorption of the food that is consumed. A key to proper absorption is sufficient hydrochloric acid (HCl). An acidic environment is needed not only to optimize the absorption of minerals, such as zinc, iron,<sup>25,26</sup> and calcium<sup>27</sup> but is also needed for the absorption of vitamin B<sub>12</sub>. In one study, an acid-reducing drug, Prilosec,<sup>®</sup> (AstraZeneca, L.P., Wayne, Pennsylvania) was shown to decrease vitamin B<sub>12</sub> absorption, a trend that was reversed when cranberry juice, well-known for its acidity, was introduced.<sup>28</sup> This interaction between vitamin B<sub>12</sub> and Prilosec may extend to other acid-lowering drugs as well. Failure to absorb iron and vitamin B<sub>12</sub> could lead to easily preventable anemia in elderly patients, causing unnecessary

fatigue and depression. In addition, there is evidence that more than a quarter of older patients already consume less than 75 percent of the recommended daily allowance of not only vitamin B<sub>12</sub>, but of folate and vitamin B<sub>6</sub> as well.<sup>29</sup> This is certainly relevant when we view the data demonstrating that lower levels of these B vitamins, which are needed to limit production of homocysteine, correlate with both higher homocysteine levels and an increased incidence of carotid-artery stenosis.<sup>30-32</sup>

Finally, a proper acidic environment in the stomach probably aids in killing a number of bacteria that may enter our bodies contained in the food that humans eat.

### Conclusion

In summary, although aging represents a complex slowing down of the body's various systems, the free-radical theory of aging may explain the process best, because free radicals eventually damage a variety of cells and overtax the body's ability to repair itself. To prevent undue free-radical damage, it makes sense for patients to ingest supplements with key nutrients that are essential to the biochemical pathways that control free radicals as well as taking supplements with additional antioxidants as these patients age. While taking hormones, such as DHEA, may be helpful for some groups of people, the most recent evidence suggests that, by itself, this hormone is not a "fountain of youth." Finally, it is important to remember that, as our patients age, they still need to maintain an acidic environment for adequate absorption of key vitamins and minerals. Indeed, proper nutritional support will increase the chances of patients navigating this natural course successfully. □

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**Chris D. Meletis, N.D.**, serves as the dean of clinical affairs/chief medical officer, National College of Naturopathic Medicine, Portland, Oregon. **Ben Bramwell** is a third-year medical student at the National College of Naturopathic Medicine.

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