Reverse Age-Related Immune Dysfunction

Exclusive Report from Leading Anti-Aging Medical Conference

Systemic Impact of Immune Senescence

A Life-Shortening Virus That Infects Most People

Novel Methods to Restore Youthful T-Cell Function

Red and White Blood Cells Flowing Through the Bloodstream
The annual SUPER SALE enables members to obtain premium grade supplements at prices substantially below what commercial companies charge. When members buy products from the Life Extension Foundation Buyers Club, they know that the quality of the products are backed by the organization’s commitment to achieving an indefinitely extended life span. What follows are a few examples of the savings members enjoy during the SUPER SALE.

<table>
<thead>
<tr>
<th>Product Name</th>
<th>Retail</th>
<th>Member SUPER SALE</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune Senescence Protection Formula</td>
<td>$40</td>
<td>$24.30</td>
<td>60 vegetarian capsules, Item # 01905 Standardized full-spectrum Reishi mushroom extract with Cistanche extract to regulate the immune system and restore youthful immune balance.</td>
</tr>
<tr>
<td>Super Omega-3 EPA/DHA with Sesame Lignans/Olive Fruit Extract</td>
<td>$32</td>
<td>$15.35</td>
<td>120 softgels, Item # 01482 Super purified EPA/DHA fish oil plus sesame lignans and potent olive (fruit and leaf) extract to provide critical omega-3 fatty acids and essential components of the Mediterranean diet.</td>
</tr>
<tr>
<td>AMPK Activator</td>
<td>$48</td>
<td>$29.70</td>
<td>90 vegetarian capsules, Item # 01907 Activating AMPK “turns off” many of the destructive factors of aging, enabling cells to return to their youthful vitality. Research shows that the two plant extracts contained in this formula (Gynostemma pentaphyllum and trans-tigliroside) promote AMPK activation.</td>
</tr>
<tr>
<td>Optimized Resveratrol with NAD+ Cell Regenerator™</td>
<td>$42</td>
<td>$24.30</td>
<td>30 vegetarian capsules, Item # 01930 High-potency trans-resveratrol now contains nicotinamide riboside, a novel form of vitamin B3 that supports mitochondrial health, along with pterostilbene and fisetin, which work in synergy with resveratrol to “turn on” longevity genes.</td>
</tr>
<tr>
<td>NAD+ Cell Regenerator™ Nicotinamide Riboside</td>
<td>$34</td>
<td>$17.55</td>
<td>100 mg, 30 vegetarian capsules, Item # 01904 Nicotinamide riboside is a revolutionary new form of vitamin B3, which is directly converted to NAD+, a coenzyme found in every cell that is essential for the efficient transfer of food to energy.</td>
</tr>
<tr>
<td>Super Booster with MacuGuard™ Ocular Support</td>
<td>$52</td>
<td>$32.40</td>
<td>60 softgels, Item # 01980 Just one softgel daily provides potent doses of vitamins K1 and K2, gamma tocopherol, sesame lignans, chlorophyllin, and lycopene, along with zeaxanthin, meso-zeaxanthin, lutein, and C3G for eye support.</td>
</tr>
<tr>
<td>Advanced Bio-Curcumin® with Ginger and Tumerones</td>
<td>$30</td>
<td>$18.23</td>
<td>30 softgels, Item #01808 Enhanced-absorbing BCM-95® curcumin with broad-spectrum inflammation-suppressing support.</td>
</tr>
<tr>
<td>Ultra Natural Prostate</td>
<td>$38</td>
<td>$21.60</td>
<td>60 softgels, Item # 01898 Comprehensive support for an aging prostate gland utilizing standardized lignans, plus boron and phospholipids for enhanced absorption.</td>
</tr>
<tr>
<td>Bone Restore with Vitamin K2</td>
<td>$24</td>
<td>$14.85</td>
<td>120 capsules, Item # 01727 Highly absorbable forms of calcium and boron, magnesium, zinc, and K2. (Available with or without vitamin K2.)</td>
</tr>
</tbody>
</table>

The SUPER SALE extends to February 2, 2015.

Members traditionally take advantage of the SUPER SALE to stock up on a year’s supply of their favorite supplements. To place your order, call 1-800-544-4440 or visit www.lef.org (SUPER SALE pricing available only to members in the US, Canada, and England.)

These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.
26 A VIRUS THAT ACCELERATES IMMUNE SENECE
Approximately 60 to 90% of adults are infected with cytomegalovirus. The result of chronic infection with this virus is depletion of the vital naïve immune cells that are necessary to fight new malignancies and infectious agents. Fortunately, there are steps you can take to offset the age-accelerating effects of cytomegalovirus.

40 BOOSTING IMMUNE FUNCTION IMPROVES LONGEVITY
The age-related decline in immune function is responsible for most life-shortening diseases. A critical strategy to reversing immune decline is to increase the production of naïve T-cells, which attack new bacteria, viruses, fungi, and malignancies. Scientists have identified two botanicals that restore several components of our aging immune systems, including increasing production of naïve T-cells while helping to remove nonfunctioning senescent cells that clog our internal immune-building factory.

52 ACTIVATE NATURAL KILLER CELLS TO FIGHT WINTER INFECTIONS
Natural killer (NK) cells are our first line of defense against infections. With age, our NK cells steadily decline, leaving us vulnerable to wintertime viruses. Researchers have shown that naturally derived enzymatically modified rice bran increases NK cell activity in circulating blood cells by up to 84% in laboratory studies.

66 NOVEL FORM OF VITAMIN B3 “TURNS OFF” AGING GENES
The fatigue and loss of motivation that accompanies aging is often caused by reduced levels of the compound NAD+. An innovative cell-boosting technology can maximize NAD+ benefits that include DNA repair, increased life span, and activation of anti-aging sirtuin enzymes.

76 THE AMERICAN ACADEMY OF ANTI-AGING MEDICINE CONFERENCE REPORT
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95 SUPER FOODS
Chia seeds provide six times the calcium of milk and are the richest vegan source of omega-3s. Research points to chia’s power to help prevent diseases such as cardiovascular disorders, cancer, and diabetes.
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Commercial “one-a-day” supplements provide very low potencies. The chart to the left reveals how much more potent the new Two-Per-Day is compared to the leading commercial multivitamin.

When compared to conventional “one-a-day” products, Life Extension’s new Two-Per-Day contains up to 50 times more potency of specific nutrients.

Commercial supplements often contain the cheapest form of nutrients, which fail to provide optimal benefits. For example, the 50 IU of synthetic vitamin E contained in Centrum® Silver® Adults 50+ may provide relatively little vitamin E to the bloodstream compared to the 100 IU of natural vitamin E in Two-Per-Day.

The new Two-Per-Day contains a small amount of nicotinamide riboside, a nutrient that has been shown to support mitochondrial health and promote longevity by boosting cellular NAD+ levels. The only common dietary source of nicotinamide riboside is cow’s milk. The daily dose of Two-Per-Day provides the amount of nicotinamide riboside found in almost 7 cups of milk.* Most members are taking higher (100 mg) doses in the NAD+ Cell Regenerator or the new Optimized Resveratrol with Nicotinamide Riboside.

A bottle containing 120 capsules of Two-Per-Day Capsules retails for $22. If a member buys four bottles during Super Sale, the price is reduced to $13.50 per bottle. (Item # 01914)

A bottle containing 120 tablets of Two-Per-Day Tablets retails for $20. If a member buys four bottles during Super Sale, the price is reduced to $12.15 per bottle. (Item # 01915)

Each bottle of Two-Per-Day lasts 60 days, so members can obtain the benefits of this high-potency formula for as little as $6.07 per month.

To order Life Extension Two-Per-Day Tablets or Two-Per-Day Capsules, call 1-800-544-4440 or visit www.LifeExtension.com


**Two-Per-Day provides a small amount of gamma tocopherols as part of natural mixed tocopherols, which include natural vitamin E.

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Bone Restore combines critical bone boosting nutrients into one superior formula.

Bone Restore includes highly absorbable forms of calcium and boron, along with vitamin D3, magnesium, zinc, manganese, and silicon. Bone Restore is available with or without vitamin K2 (MK-7).

The retail price for 120 capsules of Bone Restore is $24. If a member buys four bottles during Super Sale, the price is reduced to $14.85 per bottle. (Item# 01727)

The same Bone Restore formula without vitamin K2 (MK-7) is available as well. The retail price for 120 capsules is $22. If a member buys four bottles during Super Sale, the price is reduced to $12.83 per bottle. (Item# 01726)

Just four capsules of Bone Restore provide:

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Highly Absorbable Calcium</td>
<td>700 mg</td>
</tr>
<tr>
<td>(as DimaCal®, dicalcium malate, TRAACS® calcium bisglycinate chelate, calcium fructoborate)</td>
<td></td>
</tr>
<tr>
<td>Vitamin D3</td>
<td>1,000 IU</td>
</tr>
<tr>
<td>Vitamin K2 (as menaquinone-7)</td>
<td>200 mcg</td>
</tr>
<tr>
<td>Magnesium (as magnesium oxide)</td>
<td>300 mg</td>
</tr>
<tr>
<td>Boron (calcium fructoborate as patented Fruitex B® OsteoBoron®)</td>
<td>3 mg</td>
</tr>
<tr>
<td>Zinc (as zinc amino acid chelate)</td>
<td>2 mg</td>
</tr>
<tr>
<td>Manganese (as amino acid chelate)</td>
<td>1 mg</td>
</tr>
<tr>
<td>Silicon (from horsetail extract)</td>
<td>5 mg</td>
</tr>
</tbody>
</table>

Note: Those who take Super Booster or Super K usually do not need additional vitamin K2. They should order Bone Restore without vitamin K2. Those taking the anticoagulant drug Coumadin® (warfarin) should use Bone Restore without vitamin K2.

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To order Bone Restore, call 1-800-544-4440 or visit www.LifeExtension.com
How Immune Decline Hastens Aging

This has been an incredible year of scientific achievement. Even the lay public is coming to the realization that profoundly extended health spans may be just around the corner.

A concern expressed by our older members is whether they can remain alive long enough to benefit from the upcoming biomedical revolution. These health activists want to determine their areas of vulnerability to ensure they’re not overlooking a validated way to stave off disease, aging, and death.

Our work involving longevity research dates back to the 1960s. This has enabled us to gain exclusive insights into what causes people to die—people who otherwise take exceptionally good care of themselves.

A sad example of mortality vulnerability occurred in January 2014. That’s when one of our pioneer members died at the young age of 92. His intellectual contributions, spanning many decades, helped us survive withering governmental assaults aimed at censoring our ability to disseminate lifesaving information.

I can’t stop thinking that we were only weeks away from potentially saving him. I don’t want this same fate to befall other Life Extension® members.

We’ve talked before about the lethal impact of immune senescence. It occurs when our aging immune system fails to protect against cancers/infections, and instead generates excess inflammatory reactions that attack every cell in our body.

What virtually no one understands is how aging accelerates immune decline and what must be done to reverse this lethal trend.
The most common afflictions associated with normal aging are atherosclerosis, cancer, and Alzheimer’s disease. What few doctors know is that all these illnesses are related to immune senescence.

In people over age 65, the top 10 causes of death include pneumonia, influenza, and sepsis (systemic inflammation caused by severe infection). Immune senescence is a major cause of all these maladies.

As winter sets in, the term “immune system” is liberally tossed around as people seek to protect against viral infections. What the public does not yet understand is what causes our immune system to fail as we age.

Why Young Children Catch So Many Colds

Young children get lots of colds. Some suffer as many as eight to ten each year before age 2.

The reason youngsters suffer more colds than older children and adults is because they haven’t built up “immunity” to cold viruses. But what does this immunity really mean?

When one is exposed to an infectious agent, the body creates and maintains “memory T-cells” that provide a degree of immunity to the same infection. This works magnificently well in our first four to five decades of life. But then something happens that leads to the downward spiral of immune senescence.

Too Many “Memory T-Cells”

Memory T-cells form when our immune system successfully eradicates an invader. They remain in the body and are ready to instantly respond when that same bacteria, virus, or cancer cell reappears.

One would think it desirable to have lots of memory T-cells. The problem is that memory T-cells only work against prior infections. As we age, we collect excess numbers of memory T-cells and produce fewer critically important naïve T-cells.

The term “naïve” may not sound like something beneficial as it relates to immune function, but it is. A naïve immune cell is one that has not been activated by an antigen (a substance that provokes an adaptive immune response). Since it is “naïve” (not yet exposed to an antigen), naïve immune cells are primed to effectively respond to new infectious agents and malignancies.

Once exposed, naïve immune cells become memory cells or plasma cells specific to the original antigen. As our internal reservoir of naïve immune cells is decreased, we have less ability to respond to new infections and malignancies.

To make matters worse, excess numbers of senescent memory cells provoke undesirable inflammatory reactions that are thought to underlie most age-related diseases including atherosclerosis, cancer, and dementia.

To put this in simplistic terms, if we are to protect against the ravages of immune senescence, we need to increase our numbers of naïve cells (“virgin” immune cells), while reducing numbers of surplus senile memory cells.

Importance Of “Functional” Natural Killer Cells

The first line of defense against virus-infected and cancer cells is our natural killer cells. Young individuals have high levels of functional natural killer (NK) immune cells, but this declines with aging.

In elderly subjects, decreased NK cell activity is associated with an increased incidence and severity of viral infections such as shingles, influenza, and cytomegalovirus (CMV). Shingles occurs when our immunity to dormant chickenpox viral infection declines. It manifests as an extremely painful skin lesion that can last for months. Influenza, commonly called the flu, is a virus that inflicts its lethal effects mostly on the elderly, who represent the largest portion of the population that suffers immune dysfunction.
Cytomegalovirus (CMV) is a chronic infection that, as you’ll discover later in this issue, may contribute significantly to degenerative disease. About 90% of older people showed history of CMV infection on lab testing compared to about 60% of the general population. Increased prevalence of CMV in the elderly is thought to lead to decreased immune surveillance.

Natural killer cells originate in the bone marrow (like other immune cells) and go through a maturation process that enables them to participate in early control of microbial infections and cancers. Healthy NK function is critical in eliminating transformed cancer cells. NK cells are also involved in the elimination of senescent cells that otherwise cause chronic inflammation.

The age-related decrease in functional NK cells is likely to have wider implications for the health of older adults than currently understood by the mainstream. If an aging person is to better manage debilitating and deadly infections and malignancies, maintaining youthful NK function is critical.

Over the course of our lifetime, our immune system becomes “exhausted.” What this refers to is the excess accumulation of worn-out memory T-cells and reduced production of vital naïve T-cells.

As people accumulate exhausted T-cells, an adverse consequence is these senile memory cells emit pro-inflammatory cytokines that exacerbate chronic inflammatory conditions. Individuals with higher levels of exhausted immune cells suffer greater mortality.

The deficit of naïve immune cells combined with overaccumulation of exhausted memory cells decreases the efficacy (antibody response) of vaccinations.

Exhausted memory T-cells are associated with increased inflammation. Inflammation is associated with increased risk of coronary heart disease, impaired vascular function, vascular inflammation, and endothelial dysfunction.

An accumulation of exhausted T-cells has been seen in persons suffering from rheumatoid arthritis and ankylosing spondylitis (an inflammatory disease of the spine).

Compelling evidence points to the accumulation of senile (exhausted) T-cells as a factor that accelerates a broad array of age-associated diseases.
More T-Helper Cells Needed

**T-helper** cells identify and tag invaders for elimination by the immune system.89

**Regulatory T-cells** tell the immune system that its job is finished and it’s time to stop the attack.69-91 A normal **balance** involves having at least one to four **T-helper** cells for each **regulatory T-cell** (regulatory T-cells are sometimes called suppressor T-cells).92

As humans age, there is an **inversion in the T-helper/regulatory T-cell ratio**.93 What this means is that too many **regulatory T-cells** form while **T-helper** cell counts drop, resulting in there being more regulatory T-cells than T-helpers. The T-helper/regulatory T-cell ratio can be considered to be a predictor of mortality.76,77,94 People with **low** **T-helper** counts and **higher** **regulatory T-cell** counts **die** sooner.

Cancer patients often present with a **low** **T-helper/regulatory T-cell ratio**.95,96 Some studies show that tumor cells secrete chemicals that turn up **regulatory T-cell** formation in order to prevent the immune system from attack-

ing cancer cells.97-99 Cancer chemotherapy dramatically lowers **T-helper** counts.100,101

To combat **immune senescence**, it is critical to **reverse** the inversion of the **T-helper/regulatory T-cell ratio**. This means **boosting** **T-helper** counts while **lowering** **regulatory T-cells**.

**Reversing Immune Senescence**

**Immune senescence** is a prime cause of debility and mortality.

Fortunately, discoveries in recent years have been shown to help **reverse** the **immune dysfunction** that plagues virtually all aging humans (and cancer patients).

Here is a summary of the six underlying causes of **immune senescence** described in this article:

- **Decrease** in **naïve immune T-cells** needed to fight new invaders.93
- **Increase** in exhausted **memory T-cells** that create chronic **inflammatory** reactions.93
- **Decrease** in functional **natural killer (NK) cell activity**.91
- **Thymus** gland atrophy that reduces T-cell function and numbers.
- **Too many regulatory T-cells** and a reduction in **T-helper** cells.
- **Excess production** of **interleukin-6**, a cytokine that promotes **inflammation**.102

The good news is that there are **proven ways to counteract** all six factors involved in senile immune dysfunction.

Most Life Extension members already take **zinc** and **DHEA**. There is evidence that these supplements can at least partially restore **thymic function** vital to transforming immune cells produced in bone marrow to mature **T-cells**.103-105 DHEA also helps suppress deadly **interleukin-6**.106,107

A breakthrough in combatting **immune senescence** has been found in a medicinal plant called **cistanche** that has been used extensively in China to treat the “ailments of aging.”108

Until recently, doctors would not have understood how **cistanche**

**“We conclude that chronic heart failure patients show a higher degree of immunosenescence than age-matched healthy controls. T-lymphocyte differentiation and interleukin-6 (IL-6) levels are increased in patients with an advanced clinical status and may contribute to disease impairment through a compromised adaptive immune response due to accelerated aging of their immune system.”**


*“Immunosenescence and Inflammation Characterize Chronic Heart Failure Patients With More Advanced Disease.”*
reverses some of the underlying causes of immune senescence.

Supplementation with *cistanche* has been shown to increase naïve T-cells and natural killer (NK) cells while decreasing memory T-cells and pro-inflammatory interleukin-6.109

One of the characteristics of people who live over 100 years is a low level of interleukin-6.

A prime reason for the severe immune disorders suffered by the elderly is the marked decrease in naïve T-cells and functional natural killer cells, with a concomitant increase in memory T-cells. *Cistanche* reverses these pathological trends that characterize immune senescence.

One way *cistanche* functions is by restoring the progenitors of peripheral naïve T-cells, which explains the increase seen in these vital cells in response to *cistanche*.109 Animals supplemented with *cistanche* have increased life spans, as would be expected by a compound that counteracts immune senescence.109

*Cistanche* is one of the most popular Chinese herbal medicines and is listed in the Chinese herbal pharmacopeias as having “anti-aging” properties.

One reason the Chinese saw such impressive therapeutic results is that *cistanche* restores one of the most prominent bone marrow biomarkers of immune cell formation called stem cell antigen-1.109 Senile bone marrow loses its ability to produce fresh naïve immune cells, which are launched into the bloodstream to differentiate into mature naïve T and natural killer cells. Bone marrow stem cell antigen-1 represents the body’s main source of naïve T-cells in the blood.109 *Cistanche* appears to have a rejuvenating effect on the bone marrow, something that is now only possible using very expensive recombinant drugs.110-112

There are other factors that weaken immune function in the elderly that *cistanche* has been shown to counteract. These will be described in depth in an article appearing in this issue.

Perhaps the most exciting finding was an open-label pilot trial of elderly people that combined a low-dose of *cistanche* (100 mg) with zinc, vitamin E, vitamin B6, fucoidan, and coenzyme Q10. Not only were markers of immune senescence reversed, but the test subjects reported improvements in quality of life, such as “*not feeling tired all the time*.” This makes sense in light of the multiple adverse effects immune senescence inflicts on the body, which includes increased levels of frailty.113,114

### Hidden Effects Of Natural Killer (NK) Cell Senescence

Natural killer (NK) cells are best known for their impact on reducing the incidence and severity of viral infections.28-31

Overlooked are studies showing vibrant NK function is crucial for the immune system to recognize and eliminate unhealthy/infected cells and dysfunctional (senile) cells.27,115 A pathologic consequence of too many senile cells is tissue/organ damage and chronic inflammation.116-119

Senile (senescent) cells reside in a state of irreversible cellular paralysis. Your body wants them to die and disappear, but they linger on for dangerously long periods. While these senile cells contribute nothing to healthy function, they remain metabolically active, secreting an array of dangerous growth factors and pro-inflammatory cytokines.

Functional NK cells can eliminate senile cells before they buildup to lethal levels. When NK cells are hampered by aging, however, they are less able to remove deadly senile cells from our bodies.

As NK cells themselves become senescent in older people, there is increased reactivation of tuberculosis and viral illnesses (such as shingles and CMV), slow resolution of inflammatory responses, and increased incidence of bacterial/fungal infections and malignancies.27,120

It is likely that the senescence of NK cells has wider implications on the health of older adults than originally thought. NK cell senescence thus represents a dagger of vulnerability that predisposes us to premature suffering and death. It must be reversed to avert degenerative disease.
How To Take Advantage Of Novel Immune Restorative Technologies

Unlike prescription drugs or even certain dietary supplements, cistanche does not cost a lot. It has been added to the most popular nutrient members now take to bolster immune function (Reishi). Virtually every person over 35 should add this cistanche/Reishi immune protection duo to their daily regimen.

Another supplement to consider for short-term use is enzymatically modified rice bran, which has been demonstrated to have overwhelming benefits in boosting natural killer cell activity. The problem we have with this supplement is its high cost. What we are going to suggest, and will provide a rationale for, is for members to take this enzymatically modified rice bran for only four months out of the year.

We believe the substantial boost in natural killer cell activity will help eliminate virus-infected cells, premalignant cells, and senile cells that linger in the body and emit constant streams of pro-inflammatory cytokines. An underlying cause of aging is the accumulation of senile (senescent) cells that fail to undergo apoptosis (natural cell cycle destruction).

An increase in natural killer (NK) activity can help purge the body of these unwanted senescent cells. You’re also going to learn in this issue of Life Extension magazine why removing cells infected with the CMV (cytomegalovirus) can result in a meaningful extension of the healthy human life span.

To further restore a more youthful immune profile, we’re recommending that members go on a 60-day course of an over-the-counter drug called cimetidine. This can be purchased at pharmacies at very low cost. We suggest that most people take 800 mg of cimetidine each night for 60 consecutive days to reduce excess regulatory T-cell counts and increase T-helper cell counts. Regulatory T-cells sometimes turn off the immune system before immune eradication of virus-infected cells and tumor cells occurs.

We think this 60-day cycle of cimetidine should be considered a few times during the year, but do not take it all the time. We don’t have the data yet to support everyday use of cimetidine in protecting against immune senescence, but there is compelling evidence for shorter-term use. Cimetidine is approved by the FDA for use in heartburn sufferers (The brand name of this drug is Tagamet®.)

A trial was done on colorectal cancer patients who used 800 mg a day of cimetidine for one year. In these patients, cimetidine demonstrated significant survival benefits—84.6% of the cimetidine/fluorouracil group were alive after 10 years compared to only 49.8% of the control group (given fluorouracil alone). Life Extension has recommended cimetidine to certain...
cancer patients since 1985, and the most robust benefits have been shown to occur when cimetidine is administered prior to surgery and other immunosuppressive cancer therapies.\textsuperscript{138-142}

We urge members to get on a 60-day cycle of cimetidine now to bolster defenses against immune senescence and winter infections. On page 33 of this issue is a listing of cimetidine side effects and contraindications.

\textbf{We’re On The Verge Of Something Big…}

In case you have not figured it out yet, we are entering a new paradigm in the prevention and reversal of age-related disease.

While certain nutrients Life Extension members have taken for decades help protect against immune decline, never before have we had such an arsenal to counteract the multiple underlying factors that characterize immune senescence. And this is just the beginning.

We are funding aggressive clinical research involving bone marrow rejuvenation with the objective of mobilizing hematopoietic stem and progenitor cells (HSPCs) that will rejuvenate every tissue of our aging bodies.

We are going even further in helping the very elderly with a research project that involves taking stem cell-stimulated blood of individuals under age 25, tissue-type matching it to elderly individuals, separating the youth factors from this young blood, and transfusing it into the elderly subjects. The objective of this research project is nothing short of meaningful age reversal in individuals who may have only a few more months or years to live.

How is this expensive research funded? By the dietary supplements you purchase from the \textit{Life Extension Buyers Club}. We use proceeds from supplement sales to fund a wide range of projects aimed at finding cures for cancer, vascular disease, aging, and death itself. A record number of media stories this year highlighted areas of research we pioneered that are now being studied at prestigious universities.

\textbf{Obtain Latest Formulations At Discount Prices}

Once a year, we discount the price of every one of our advanced nutritional formulas. Members take advantage of this once-a-year \textbf{Super Sale} to stock up on their favorite supplement formulas.

What should comfort members more than anything else are the three novel methods to counteract aging we have introduced over the past few months. In addition to the immune senescence reversal program discussed in this editorial, there is now a supplement that mimics several of the longevity properties of the drug \textit{metformin}, and a cell-regenerating nutrient called \textit{nicotinamide riboside} that we’ve been working on since the year 2001.

We’ve also combined some nutrients into existing formulas so that members can obtain more benefits while swallowing fewer pills.

No organization in the world is combatting senescence and human mortality more aggressively than \textit{Life Extension}. Your support via supplement purchases and donations enables us to expand on an unprecedented biomedical research endeavor:

To order nutrients you need today at \textbf{Super Sale} prices, call 1-800-544-4440.

For longer life,

\[\text{William Faloon}\]
Premature Death Of Jack LaLanne
Likely Caused By Immune Senescence

It is impossible to overstate the magnitude of disability and death that immune senescence inflicts on aging human populations. When you hear a person died from “old age,” in almost every instance the underlying culprit is a dysfunctional immune system that ignites deadly inflammatory fires while failing to protect against infections and malignancies.

No one we know tried to live for over 100 years more than health pioneer Jack LaLanne. He engaged in rigorous lifelong exercise and ate a low-calorie healthy diet. He followed an old-line supplement program probably devoid of vitamin K and DHEA, which may have contributed to his premature death at age 96.

Jack LaLanne died of pneumonia following aortic valve surgery. Aortic valve stenosis is caused by calcification, chronic inflammation, and other factors such as elevated homocysteine.143

Vitamin K prevents calcification that is so often the reason why an elderly person’s aortic valve fails.144-145 DHEA partially protects against inflammation.150-152

Immune senescence may very well have contributed to Jack LaLanne’s early demise by crippling his ability to fight off the pneumonia, which was the acute cause of his death.

It is difficult to imagine someone as fit and vigorous as Jack LaLanne succumbing to pneumonia. Yet a dysfunctional immune system deprives even the hardiest of us from warding off infections that were easily overcome in our youth.

Clearly, protecting against immune senescence is a mandatory component of a longevity program.

References

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The optimal dose of PQQ is 20 mg each day. Members taking Mitochondrial Energy Optimizer, Mitochondrial Basics, or PQQ 10 mg caps obtain this optimal PQQ dose when taking the new Super Ubiquinol CoQ10 with BioPQQ®.

Super Ubiquinol CoQ10 with BioPQQ® energizes and generates new mitochondria in aging cells!

Super Ubiquinol CoQ10 with BioPQQ® contains shilajit to increase coenzyme Q10 in mitochondria plus PQQ to support the generation of new mitochondria in aging cells. This three-way mitochondrial support strategy offers the following benefits:

1. **Ubiquinol CoQ10** - CoQ10 is required for generating optimal cellular energy. The ubiquinol form of CoQ10 offers superior absorption compared to the standard ubiquinone form.

2. **Shilajit Complex** - PrimaVie® Shilajit has been shown to double levels of CoQ10 in the mitochondria. Combining CoQ10 and Shilajit produced a 56% increase in energy production in the brain and a 144% increase in energy production in muscle.

3. **BioPQQ®** - PQQ activates genes that promote the formation of new mitochondria while boosting mitochondrial antioxidant defenses.

A bottle of 30 softgels of Super Ubiquinol CoQ10 with BioPQQ® retails for $54. If a member buys four bottles during Super Sale, the price is reduced to $31.05 per bottle.

**References**


Kaneka QH Ubiquinol® is a registered trademark of Kaneka Corporation. PrimaVie® is a registered trademark of Natreon, Inc. BioPQQ® is a registered trademark of MGC (Japan).

To order Super Ubiquinol CoQ10 with BioPQQ®, call 1-800-544-4440 or visit www.LifeExtension.com

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.
AMPK is an enzyme that serves as the body’s “master regulating switch.” It inhibits multiple degenerative factors by revitalizing aging cells. Found in every cell, AMPK promotes longevity factors that have been shown to extend life span in numerous organisms. Increasing AMPK signaling “turns off” many destructive effects of aging, thus enabling cells to return to their youthful vitality.

Life Extension® scientists have compiled years of research to create AMPK Activator, a specialized dual-extract formulation that supports AMPK activation for health optimization. This natural formula supports AMPK enzymatic activities required to safely support a more youthful cellular environment.

Importance Of AMPK
Greater AMPK (adenosine monophosphate-activated protein kinase) activation has been shown to help target damaging factors of aging. Studies show increased AMPK activity supports reduced fat storage, new mitochondria production, and the promotion of healthy blood glucose and lipids already within normal range.

Gynostemma Pentaphyllum
An extract of the plant Gynostemma pentaphyllum was traditionally used in Asian medicine to promote longevity and scientists now know why—G. pentaphyllum promotes AMPK activation! In one of many studies showing a wide variety of benefits, researchers documented a 1-inch reduction in abdominal circumference in overweight individuals who took 450 mg daily of G. pentaphyllum extract for 12 weeks.

Trans-Tiliroside
Trans-tiliroside, extracted from plants such as rose hips, also boosts AMPK activation, but triggers different downstream metabolic benefits than G. pentaphyllum. Among its many benefits, a low equivalent dose of 56 mg daily trans-tiliroside has been shown by researchers in preclinical studies to promote healthy blood glucose levels and body weight already within normal range.

References

To order AMPK Activator at low Super Sale prices, call 1-800-544-4440 or visit www.LifeExtension.com

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.
Super Booster

Most people don’t get enough oil-based nutrients from their diet. Super Booster solves that problem with a once-a-day softgel that provides high potencies of fat-soluble nutrients and other compounds.

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.
Walnuts May Provide Brain Benefit In Alzheimer's Patients

According to an article that appeared in the *Journal of Alzheimer's Disease*, a diet enriched with walnuts can help slow down, or even prevent, Alzheimer's disease.*

Researcher Abha Chauhan, PhD, and associates say an extract in the nuts may provide a protective effect against oxidative damage caused by beta-amyloid protein. A build-up of this protein leads to beta-amyloid plaque, which is believed to play a major role in the development of the disease.

Over a period of nine to 10 months, the team fed 4-month-old Alzheimer's-induced transgenic mice a diet containing 6 or 9% walnuts, which is the equivalent of 1 or 1.5 ounces of walnuts per day in humans. Control groups consisting of transgenic mice and regular mice were fed a walnut-free diet. Between the ages of 13 and 14 months, all animals were tested for spatial memory and learning ability, position discrimination learning ability, psychomotor coordination, and anxiety-related behavior.

The transgenic mice on a control diet exhibited increased memory deficit and anxiety-related behavior, and impairments in spatial learning ability, position discrimination learning ability and motor coordination in comparison with normal mice on the same diet. The animals that ate the walnuts showed improvements in memory, learning, anxiety and motor development compared to the transgenic controls.

*Editor's Note:* In light of the significant amount of inflammation present in Alzheimer's disease, the researchers suggest the high omega-3 fatty acid content in the nuts could be responsible for the benefits observed.


Resveratrol Shows Bone Benefit

A study published in the *Journal of Clinical Endocrinology & Metabolism* found that resveratrol improved spinal bone density in men with metabolic syndrome—a cluster of risk factors associated with an increased risk of cardiovascular disease and diabetes—and may provide potential as a treatment for osteoporosis.*

Sixty-six obese men received 500 mg resveratrol, 75 mg resveratrol, or a placebo twice daily for 16 weeks. Bone mineral density, geometry, and microstructure were assessed before treatment and at the study's conclusion. Bone alkaline phosphatase and other blood markers of bone formation were measured at baseline and at four, eight, and 16 weeks.

Participants who received the resveratrol experienced a 2.6% increase in lumbar spine volumetric bone mineral density at the end of the study and an average 16% increase in bone alkaline phosphatase in comparison with the placebo group at each time point measured.

*Editor's Note:* "Our study is the first to reveal resveratrol's potential as an anti-osteoporosis drug in humans," announced lead author Marie Juul Ørnstrup, MD, of Aarhus University Hospital in Denmark. "Our findings suggest the compound stimulates bone-forming cells within the body."

*J Clin Endocrinol Metab. 2014 Oct 16.*
Acute Glaucoma Is An Inflammatory Disease

A study published in *Proceedings of the National Academy of Sciences* found that loss of vision in mice suffering from acute glaucoma, an inflammatory disease, can be caused by high pressure in the eye that sets in motion an inflammatory response leading to death of retinal cells.*

In the study, scientists at UC San Diego School of Medicine and Sun Yat-Sen University in China proved that a large, rapid, and sustained increase in eye pressure switched on a gene (TLR4) that activated a protein called caspase-8. Caspase-8 triggers the production of inflammatory proteins that typically allow mammals to fight microbial infections. By suppressing either the TLR4 gene or caspase-8 protein, the researchers were able to slow retinal cell death in mice with glaucoma.

"This immune response is a double-edge sword because, while these proteins protect us from infection in a normal situation, they stimulate apoptosis (programmed cell death) in retinal cells in cases of acute glaucoma," said study co-author Dr. Kang Zhang, of UC San Diego School of Medicine.

Editor’s Note: By 2020, an estimated 3 million Americans will be diagnosed with glaucoma, the second leading cause of blindness. The study results will have immediate and broad clinical importance regarding the treatment of the disorder.

* *Proc Natl Acad Sci.* Epub 2014 July 14.

Higher Potassium Intake Linked With Lower Risk Of Death, Stroke

The finding of a reduced risk of stroke and premature mortality among women with a higher intake of potassium was reported in the journal *Stroke.*

The current investigation utilized data from 90,137 postmenopausal women who had no history of stroke upon enrollment in the Women’s Health Initiative Observational Study. Dietary questionnaire responses were analyzed for potassium intake, which averaged 2,611 mg per day. Over an average 11-year follow-up period, 3,046 strokes (including 2,190 ischemic strokes) occurred and there were 11,596 deaths from all causes.

Among women whose potassium intake was among the highest 25%, there was a 12% lower risk of stroke, a 16% lower risk of ischemic stroke, and a 10% lower risk of dying from any cause over follow-up in comparison with those whose intake was among the lowest 25%.

Editor’s Note: Although the US Department of Agriculture recommends a level of 4,700 mg of potassium daily, lead researcher Dr. Sylvia Wassertheil-Smoller, of the Albert Einstein College of Medicine, New York, observed that, “Only 2.8% of women in our study met or exceeded this level. The World Health Organization’s daily potassium recommendation for women is lower, at 3,510 mg or more. Still, only 16.6% of women we studied met or exceeded that.”

* *Stroke.* Epub 2014 Sep 4.

Decreased Arterial Stiffness Associated With Supplementation

The results of a meta-analysis published in the *Journal of Nutrition* indicate that supplementing with nutrients could help protect against arterial stiffening that occurs with aging.*

Ammar W. Ashor and colleagues at England’s Newcastle University selected 20 randomized trials that included a total of 1,909 participants aged 22 to 63 for their analysis. Studies involved vitamin C and/or E alone, or a combination of other vitamins and/or mineral supplementation. Arterial stiffness was evaluated via pulse-wave velocity measurement or other methods.

Pooled analysis of the data revealed a significant reduction in arterial stiffness associated with supplementation in comparison with a placebo or no treatment. The benefit was more pronounced in studies in which arterial stiffness was experimentally induced or in primary prevention trials, and was stronger among those with lower plasma vitamin C and E prior to supplementation.

Editor’s Note: “The beneficial effects of vitamins on vascular stiffness may be explained by the reduction of the damaging effects of free radicals on structural and functional components of the vessel walls,” the authors said. “Vitamins inactivate free radicals, reduce inflammation, and therefore protect the integrity of the vascular wall. Furthermore, vitamins increase the bioavailability of the vasodilator and anti-inflammatory molecule nitric oxide.”

Deficient Vitamin D Levels Associated With Greater Risk Of Dying From Sepsis Or Septic Shock

Researchers at Detroit’s Henry Ford Hospital report a protective effect of having sufficient vitamin D levels against the risk of dying from sepsis or septic shock within 30 days of intensive care unit admission. The findings were reported in the September 2014 issue of the American Journal of Critical Care.*

The study included 121 men and women admitted to the hospital’s ICU with severe sepsis or septic shock, an inflammatory state resulting from infection in the bloodstream. Blood samples obtained before or during admission were analyzed for serum 25-hydroxyvitamin D levels. Vitamin D deficiency, categorized in this study as a level of 15 ng/mL or less, was uncovered in 54% of total patients. Thirty-seven percent of vitamin D-deficient subjects died from any cause within 30 days of admission, in comparison to 20% of those who were not deficient.

Editor’s Note: “Mortality may be decreased by ensuring adequate vitamin D concentrations through supplementation with ergocalciferol or cholecalciferol within 30 days of hospitalization,” the authors write. “This finding has important implications because sepsis is a leading cause of mortality in critically ill patients.”

Low-Dose Aspirin Linked To Decreased Blood Clot Risk

A study published in Circulation affirmed that regular intake of low-dose aspirin may help reduce the incidence of recurrent venous blood clots referred to as venous thromboembolism, as well as the risk of cardiovascular events.*

For the current study, Dr. John Simes, of the University of Sydney, Australia, and fellow researchers analyzed data from the WARFASA (Warfarin and Aspirin) and ASPIRE (Aspirin to Prevent Recurrent Venous Thromboembolism) trials. Participants in both trials received 100 mg aspirin or a placebo daily for a median period of 24.2 months.

Among 1,224 men and women included in the combined analysis, venous thromboembolism occurred in 18.4% who received a placebo and 13.1% assigned to aspirin, resulting in a 32% reduction among aspirin users. Subjects who received aspirin additionally experienced a 34% reduction in the risk of major vascular events, including symptomatic venous thromboembolism, heart attack, stroke, and cardiovascular death, in comparison with the placebo group. The risk of clinically relevant bleeding was not significantly different between the two groups.

Editor’s Note: “The treatment effect of aspirin is less than can be achieved with warfarin or other new generation direct thrombin inhibitors, which can achieve more than an 80% reduction in adverse circulatory and cardiopulmonary events,” Dr. Simes noted. “However, aspirin represents a useful treatment option for patients who are not candidates for anticoagulant drugs because of the expense or the increased risk of bleeding associated with anticoagulants.”


Watch Out For Watchful Waiting

Findings from a study reported in Urologic Oncology indicate that watchful waiting, a no-treatment strategy recommended to many older men with low-grade prostate cancer, may not be appropriate for all patients, particularly African Americans.* “We know that African American men have more aggressive prostate cancer than Caucasian men,” noted lead researcher Kosj Yamoah, MD, PhD.

Dr. Yamoah and associates evaluated data from a group of men with low to intermediate grade cancer as indicated by Gleason scoring of biopsy samples obtained by surgical removal of all or part of the prostate gland. (Restricting the study to men who underwent surgical removal of tissue for biopsy rather than needle biopsy samples helped ensure the accuracy of the tumor grading process by reducing the chance of missed areas of aggressive disease.) Over a seven-year period, disease control was observed in 90% of Caucasian men as opposed to 79% of African American men.

Editor’s Note: “Our study shows that African American men who are diagnosed with a low-grade cancer at first—the cancers that are sometimes watched rather than treated—are more likely to develop aggressive disease sooner than Caucasian men,” Dr. Yamoah concluded.

* Urol Oncol. Epub 2014 Sep 8.

Resveratrol Reduces High-Fat Diet’s Effects On Mitochondrial Function

The Journal of Food Science reports the finding of a beneficial effect for resveratrol in preventing the adverse effects of a high-fat diet on mitochondrial function and other factors.*

Researchers divided 24 mice to receive a normal diet, a high-fat diet, or a high-fat diet enhanced with 0.06% resveratrol for 20 weeks. At the end of the experiment, blood and spleen cell samples were analyzed for regulatory T-cell counts and other factors.

While regulatory T-cells in blood and spleen were reduced by the high-fat diet, their survival was improved in animals that received resveratrol. Resveratrol was also associated with a decrease in the elevation of reactive oxygen species production and restoring loss of mitochondrial function that was observed in the regulatory T-cells of high fat diet-fed animals. Resveratrol was found to increase the expression of a regulator of mitochondrial biogenesis and reduce regulatory T-cell apoptosis.

Editor’s Note: “High-fat diet is a significant risk factor for health, and mitochondrial dysfunction is one of the major events activating cell death pathways during high-fat diet-induced oxidative stress,” writes Bin Wang, of China’s School of Food Science and Technology in Jiangsu. “We have already reported that several immune functions were changed in mice by high-fat feeding, indicating that the proinflammatory state of obese individuals might be related to chronic excessive nutrient intake.”

Validated in Huge New Study: Vascular Benefits of a Mediterranean Diet

A large, rigorous study published in the *New England Journal of Medicine* confirmed the health benefits of those who switch to a Mediterranean diet rich in omega-3 fatty acids as well as protective nutrients called polyphenols found in olive oil, fruits, vegetables, nuts like walnuts, and wine. The study ended early because the life-sparing effects were so overwhelming, with startling benefits for vascular health.

In addition to health-promoting vegetables and fruits with their abundance of polyphenol nutrients, the Mediterranean diet group also took 4 tablespoons of polyphenol-rich extra-virgin olive oil a day.

**Life Extension® Members Benefited Long Ago**

Starting in 2005, Life Extension members began taking a supplement (Super Omega-3) that provided potent concentrations of fish oil and olive polyphenols like hydroxytyrosol and oleuropein.

Olive oil contains polyphenol nutrients that have demonstrated wide-ranging health benefits. The recommended daily dose of Super Omega-3 supplies a similar polyphenol content to that found in 4 to 6 tablespoons of olive oil.

This supplement also provided standardized sesame lignans to support the beneficial effect of omega-3 fatty acids in the body.

The sesame lignans not only direct the omega-3s fatty acids toward more effective pathways in the body, but guard the delicate fish oil from oxidation.

**CAUTION:** If you are taking anticoagulant or antiplatelet medications, or have a bleeding disorder, consult your healthcare provider before taking this product.

Supportive but not conclusive evidence shows that consumption of EPA and DHA omega-3 fatty acids may reduce the risk of coronary heart disease. IFOS™ certification mark is a registered trademark of Nutrasource Diagnostics, Inc. These products have been tested to the quality and purity standards of the IFOS™ program conducted at Nutrasource Diagnostics, Inc.

**Super Omega-3 with Sesame Lignans and Olive Fruit Extract**

To ensure the purest, most stable, and easy-to-tolerate fish oil, Super Omega-3 EPA-DHA is molecularly distilled. It enjoys the highest 5-star rating for purity, quality, and concentration from the renowned International Fish Oil Standards program.

A bottle containing 120 softgels of Super Omega-3 EPA/DHA with Sesame Lignans & Olive Fruit Extract retails for $120. If a member buys four bottles during Super Sale, the price is reduced to $100 per bottle. If 10 bottles are purchased during Super Sale, the cost is $15.35 per bottle. (Item #01482)

**The daily dose (four regular size softgels) of Super Omega-3 EPA/DHA with Sesame Lignans & Olive Fruit Extract provides:**

- EPA (eicosapentaenoic acid) 1,400 mg
- DHA (docosahexaenoic acid) 1,000 mg
- Typical DPA (docosapentaenoic acid) 156 mg
- Olive Extract (fruit and leaf) providing 39 mg polyphenols, 10.4 mg hydroxytyrosol/tyrosol, 8.8 mg verbascoside/oleuropein)
- Sesame Seed Lignan Extract 20 mg

**References**


To order the most advanced fish oil supplement, Super Omega-3 EPA/DHA with Sesame Lignans and Olive Fruit Extract (with or without enteric coating), call 1-800-544-4440 or visit www.LifeExtension.com

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.
A major reason why our immune system fails with aging is that we lose vital naïve (virgin) immune cells while we accumulate excess levels of senile memory cells.¹²

Naïve immune cells are needed to respond to new malignancies and infectious agents,³ whereas memory immune cells only respond to the original antigen, i.e. bacteria, virus, or cancer cell.⁴

Once our reserve of naïve immune cells is depleted, we become vulnerable to diseases that were fought off in our youth. Some people suffer accelerated immune senescence that wreaks havoc throughout their body. These individuals are unable to fend off new invaders because of naïve cell depletion. They may also suffer systemic damage caused by inflammatory signals emitted from senescent memory cells.¹

A growing body of evidence has identified a virus (cytomegalovirus) that causes us to more rapidly deplete vital naïve immune cells with the consequential buildup of excessive memory cells.¹

A disconcerting 60 to 90% of us are estimated to harbor this insidious virus.⁵ Fortunately, there are steps one can take to help offset the age-accelerating effects inflicted by the cytomegalovirus (CMV) and thus retain more youthful immune function.
There is a limit as to how many naïve immune cells our bodies normally produce and this number declines with age.\textsuperscript{6-9} Once a naïve cell is exposed to an antigen, it converts to a memory type immune cell that only responds to the same virus, bacteria, or other foreign agent.\textsuperscript{4,10}

When we develop certain chronic viral infections, our immune system goes into constant overdrive, producing high levels of naïve cells that convert into memory cells upon exposure to new copies and strains of the virus replicating in our cells. Unfortunately, there are only limited numbers of these vital naïve immune cells our bodies can naturally make.

Those inflicted with HIV suffer an accelerated form of aging as their immune system works to fight the virus, despite the advent of anti-HIV drugs.\textsuperscript{11,12} Hepatitis C infection creates this same problem.\textsuperscript{13} The breakthrough news about hepatitis C is that new drugs are curing up to 90\% of those infected.\textsuperscript{14}

Most of us, however, are not infected with hepatitis C or HIV. What the vast majority of us do harbor in our bodies is the cytomegalovirus. Lab tests revealed that it is present in approximately 60\% of the general population, and in 90\% of those over the age of 80.\textsuperscript{5}

The insidious property of cytomegalovirus (CMV) is that it leads to the continuous production of viral proteins that have the ability to establish secondary infections with differing CMV strains.\textsuperscript{15-17} The deadly consequence that has been observed is continuous stimulation (and subsequent depletion) of naïve cells and excess accumulation of dysfunctional memory cells leading to the development of accelerated immune senescence.\textsuperscript{18-20}

Unless one is immune compromised, most of us infected with CMV are asymptomatic—or so we think.\textsuperscript{21} The harsh reality is that chronic CMV infection is associated with frailty, cognitive decline, and arterial occlusion—hallmark pathologies of “normal” aging processes.\textsuperscript{22,23}

CMV Shown To Shorten Life Span

CMV infection can increase mortality (death) rate in otherwise healthy older individuals. This is most clearly seen by an increase in vascular deaths and immune senescence.\textsuperscript{22,24}

One study found that high CMV antibody levels (associated with CMV exposure) were independently associated with a 179\% greater mortality rate over a five-year period.\textsuperscript{22} Another study showed a 35\% increase in cardiovascular disease mortality in those with elevated CMV indicators.\textsuperscript{25} In still another study, CMV reduced life expectancy by 3.7 years after adjusting for other factors.\textsuperscript{24}

What scientists are finding is that chronic CMV infection “exhausts” the immune system. It does this by depleting naïve cells needed to ward off new CMV strains and leaving behind a large population of pro-inflammatory senile memory cells.\textsuperscript{18,26}

Of interest, however, was a study on long-lived family members whose offspring enjoy a 30\% reduced mortality rate.\textsuperscript{27} These rare individuals, genetically enriched for longevity, were less susceptible to the characteristic CMV-driven impairments of immune function. This study showed that CMV infection was strongly associated with an age-related reduction in vital naïve T-cells and accumulation of memory T-cells in the general population, but not in members of long-lived families.\textsuperscript{27} These long-lived individuals also showed lower pro-inflammatory status as measured by C-reactive protein. This study implies that by initiating strategies to boost naïve T-cell populations and suppress excess memory cells, one might derive some of the enhanced longevity benefits enjoyed by genetically programmed long-lived individuals.

CMV Adversely Affects
Cognitive Thinking

T-helper cells are needed to help initiate an immune attack against foreign invaders. Regulatory T-cells (also known as suppressor T-cells) turn down immune responses, preferably after the pathogen has been brought under control.\textsuperscript{28}
For optimal immune health, one should have approximately one to four T-helper cells for every one regulatory T-cell.29,30 As a result of normal aging, regulatory T-cell counts elevate,31,32 while T-helper counts decline.33 Certain cancers appear able to boost regulatory T-cell counts in order to protect themselves against an immune attack.34-36

A study published in 2014 evaluated 360 adults (aged 60-103) and found that those with higher CMV activity had an 8-fold increased risk of an inverted T-helper/regulatory T-cell ratio, meaning they had more regulatory T-cells than T-helpers.37 These human study subjects with inverted T-helper/ regulatory T-cell ratios had impairments in some cognitive dimensions and more functional disability and dependency compared to subjects with higher T-helper counts and lower regulatory T-cell counts.

Humans with lower T-helper counts and higher regulatory T-cell counts die sooner.38 It is thus important for aging individuals and certain cancer patients to take aggressive steps to maintain higher youthful levels of T-helper cells and keep regulatory T-cell counts from increasing too much.

How CMV Inflicts So Much Damage
CMV attacks the endothelial lining of our arteries, which explains the high prevalence of vascular death seen in those with active CMV infection.39-45 Immune cells are highly dependent on telomerase activity in order to maintain youthful function.46 CMV causes immune cells to lose telomerase activity.47-49 CMV also forces vital naïve immune cells to be used to suppress active infection. The result is accelerated immune senescence.50-52 As naïve immune cells decline, aging humans lose their natural protection against bacteria, viruses, and cancer.

Naïve cells are lost to normal aging, making CMV infection particularly deadly in the elderly.24,53 Active CMV infection is present in virtually all glioblastoma (fatal brain tumor) patients.54 As we reported in 2013, administering an anti-CMV drug (valganciclovir) to glioblastoma patients improves two-year survival rates by more than 3-fold.55 However, this drug has side effects56,57 and costs about $50,000 annually. It is thus not yet suitable for most normal aging people.

Another way to suppress CMV may be to bolster natural killer cell activity. An important function of natural killer (NK) immune cells is to destroy virus-infected cells throughout our body.58

CMV May Speed Up Immune Senescence

- An aging immune system fails because, as we age, the body loses vital naïve immune cells and accumulates excess levels of senescent memory cells.
- This makes us vulnerable to diseases that were easily overcome in youth.
- Growing evidence shows that a virus called cytomegalovirus (CMV) depletes naïve immune cells and infects approximately 60 to 90% of people.
- CMV infection can shorten the life span of otherwise healthy older adults. Bolstering natural killer cell (NK) activity may suppress CMV.
- A four-month course of a compound called enzymatically modified rice bran, along with a 60-day course (800 mg/day) of an over-the-counter drug called cimetidine, can help reduce the CMV burden in the body and boost antiviral activity.
- A commonly used Chinese herbal extract called cistanche can also influence antiviral components and help increase naïve T-cells and NK cells.
An effective defense against CMV in immune competent subjects requires the participation of NK cells and T-lymphocytes... It has been shown that CMV chronic infection in old individuals is associated with accumulations of late-differentiated CD8 T-cells, characteristic of CD8 T-cell immunosenescence, and with the development of an ‘Immune Risk Phenotype’ (IRP), predictive of early mortality in the elderly indicating that this virus is a major driving force of T-cell immunosenescence.”


An Immune Cell That Destroys CMV

Cytomegalovirus (CMV) invades cells throughout the body and spews out copies that infect other cells.83 The first line of defense against virus-infected and malignant cells is our natural killer (NK) cells.84-87 Young individuals have high levels of functional natural killer immune cells, but this declines with aging.88-90

In elderly subjects, decreased NK cell activity is associated with an increased incidence and severity of viral infections, which explains why 90% of older people show CMV infection compared to about 60% of the general population.5 Healthy NK function is critical in eliminating transformed cells before a viral infection or malignancy develops.59,91,92 NK cells are involved in immune regulation, antimicrobial immune responses, and elimination of senescent cells that otherwise cause chronic inflammation.59

The age-related decrease in healthy NK cell function is critical in eliminating transformed cells before a viral infection or malignancy develops.59,91,92 NK cells are involved in immune regulation, antimicrobial immune responses, and elimination of senescent cells that otherwise cause chronic inflammation.59

The age-related decrease in healthy NK cell function is likely to have wider implications for the health of older adults than currently understood by the mainstream. If an aging person is to control debilitating and deadly CMV replication, maintaining more youthful NK function would appear to play a critical role, as would restoration of the naïve immune cell population.

CMV-Induced Immune Cell Exhausiton

Immune cells used to suppress chronic infections like cytomegalovirus (CMV) become senile or “exhausted” over time.18,50,59,60

As people accumulate exhausted T-cells, an adverse consequence is that the senile cells emit pro-inflammatory cytokines that exacerbate the chronic inflammation observed in elderly persons.61,62 These individuals suffer higher mortality.63,64

The deficit of naïve immune cells combined with overaccumulation of exhausted T-cells decreases the efficacy (antibody response) of vaccinations.65-67

Persistent CMV infection and the consequent accumulation of pro-inflammatory exhausted T-cells are associated with increased risk of coronary heart disease, impaired vascular function, vascular inflammation, and endothelial dysfunction.39,41,68-72 This all leads to increased blood pressure and contributes to atherosclerosis.73

An accumulation of exhausted T-cells has been seen in persons suffering from rheumatoid arthritis and other chronic inflammatory conditions.74,75

A strong body of evidence, mostly published over the past few years, indicates that persistent CMV infection and the accumulation of senile (exhausted) T-cells initiates and accelerates a broad array of age-associated and inflammatory diseases.76-81
Since we know that **NK cells** hunt down virus-infected cells and eliminate them, it makes sense to take steps to boost the **functionality** of our aging **NK cells** to suppress CMV activity.

Enhanced NK cell function alone will not likely eradicate CMV, but it can downregulate active CMV infection to reduce the damage inflicted on the body and theoretically reduce the number of **naïve immune cells** that will be used up fighting it.\(^{103}\)

In as much as aging itself causes a decline in functional **NK activity**, initiating a four-month course of an NK-boosting compound like **enzymatically modified rice bran** offers an intriguing approach to reducing the CMV burden in an aging body.\(^{104-106}\)

To further boost antiviral activity, consider taking **800 mg** each night of the over-the-counter drug **cimetidine** for 60 continuous days. This drug is approved for relieving heartburn, but a side benefit is that it boosts the number of **T-helper immune cells** while suppressing excess **regulatory T-cells**.\(^{107-110}\)

**Suppressing CMV Infection**

Immune compromised people, such as HIV patients, organ transplant recipients given immune-suppressing drugs, and certain cancer chemotherapy patients are particularly vulnerable to **acute CMV infection**.\(^{93-96}\) These individuals facing blindness, pneumonia,\(^{98}\) and possible death from an uncontrolled CMV infection are prescribed a drug like **valganciclovir** that is highly effective in controlling viral replication.\(^{99-101}\)

One of the side effects of this drug is **bone marrow** suppression, which can hasten **immune senescence**.\(^{102}\) That’s because immune cells are formed in our bone marrow where they are released into the bloodstream for further differentiation into specific disease-fighting cells like macrophages and NK cells. Valganciclovir is therefore not recommended for most CMV-infected individuals who are asymptomatic.

Since we know that **NK cells** hunt down virus-infected cells and eliminate them, it makes sense to take steps to boost the **functionality** of our aging **NK cells** to suppress CMV activity.

Enhanced NK cell function alone will not likely eradicate CMV, but it can downregulate active CMV infection to reduce the damage inflicted on the body and theoretically reduce the number of **naïve immune cells** that will be used up fighting it.\(^{103}\)

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As people age, and/or contract an illness such as cancer, they often produce too many **regulatory T-cells**\(^{111,112}\) that prematurely shut down needed immune activity.\(^{113-118}\) Aging also results in a **decline** of **T-helper cells** that initiate immune responses to virus-infected and cancer cells.\(^{119}\) Cimetidine can be obtained without a prescription at your local pharmacy at low cost.

**T-helper cells** are required for the immune system to react to new infections and malignancies.\(^{120,121}\) They help activate the secretion of antibodies and macrophages to destroy ingested microbes and help activate cytotoxic T-cells to kill virus-infected target cells. To fully appreciate the importance of T-helper
Aging humans who choose not to take cimetidine should still consider initiating low-cost cistanche daily, along with a four-month regimen of enzymatically modified rice bran.

Summary

The immune system begins to shut down as we age due to the loss of vital naïve immune cells and an accumulation of excess levels of older memory cells, which makes us vulnerable to disease. Research shows that about 60 to 90% of adults harbor a virus called cytomegalovirus (CMV), which depletes naïve immune cells. CMV may increase mortality in healthy older adults.

Enzymatically modified rice bran, taken over the course of four months, along with a 60-day regimen of cimetidine, may reduce CMV and boost antiviral activity. Cistanche, a common Chinese botanical extract, can also influence antiviral components and help increase naïve T-cells and NK cells.

There Is Not Yet Universal Consensus On CMV And Immune Senescence

Not all published scientific papers agree that CMV infection accelerates immune senescence. The topic is currently being debated by immunologists around the world. The studies supporting the pathologic impact of CMV on immune status are compelling, as is the data associating active CMV infection with shortened human life spans. But as critics accurately point out, “association” is not always the same as “causation.”

For an aging human concerned about their health and longevity, it does not necessarily matter if CMV is accelerating immune senescence. That’s because maturing individuals are already suffering a decline of naïve T-cells, reduced T-helper cells, loss of NK cell activity, accumulation of worn out memory cells (that emit chronic inflammatory signals), and an increase in regulatory T-cells. So initiating daily supplementation with 210 mg of cistanche, a 60-day course using 800 mg daily of cimetidine, and a four-month course using 500 mg daily of enzymatically modified rice bran makes sense for anyone over age 35 (and sometimes younger individuals with certain immune deficits).

I’m ending this article with information about cimetidine side effects. I know Life Extension® members have historically shied away from drugs because of side-effect concerns. When it comes to the 60-day course of 800 mg/day of cimetidine, I hope eligible members will take into account the many rewards that a strong immune boost provides and view drug interaction risk only as it relates to their individual status.

If you have any questions on the scientific content of this article, please call a Life Extension® Health Advisor at 1-866-864-3027.
Cimetidine: Drug Interactions And Side Effects

We describe here potential side effects for certain individuals taking cimetidine.

From past experience, I know the risk of any side effect will preclude some Life Extension members from considering even a 60-day course of cimetidine at the moderate dose of 800 mg at bedtime.

By way of analogy, I have dealt with aging men who have stubbornly high levels of C-reactive protein, which is an inflammatory factor associated with greater incidence of vascular disease, dementia, and certain cancers.127-132

Low testosterone levels are associated with higher C-reactive protein levels.133-136 An unwarranted fear of prostate cancer caused many of these men to not elevate their testosterone levels. The outcomes in some cases were tragic.

When it comes to cimetidine, the benefit is boosting T-helper immune cell counts and lowering excess regulatory T-cell levels that interfere with optimal immune defenses. Mortality rates are higher in those with surplus regulatory T-cells in relation to T-helper cell counts.

I hope members who could benefit from a 60-day course of cimetidine (800 mg a night) will not be dissuaded by side effect risks that are usually manageable if they occur at all.

Significant Drug Interactions

Cimetidine is a known inhibitor of many isozymes of the cytochrome P450 enzyme system, including but not limited to CYP2D6, 3A4 and 1A2 isoenzymes, which can cause increases in plasma concentrations of certain drugs when cimetidine is ingested.137,139

A short list of important, clinically relevant drug interactions include:102

- Warfarin (Coumadin®), an anticoagulant;
- Sildenafil (Viagra®), a PDE5 inhibitor for erectile dysfunction;140
- Phenytoin (Dilantin®), an anticonvulsant;
- Propranolol (Inderal®), a beta-blocker used to reduce blood pressure and heart rate;141
- Nifedipine (Procardia®), a Ca²⁺-channel blocker primarily used to reduce blood pressure;
- Diazepam (Valium®), an anti-anxiety medication;142

Several tricyclic antidepressant drugs, lidocaine, theophylline (anti-asthmatic) and metronidazole (antifungal).141

Dosage of these drugs and other similarly metabolized drugs, particularly in patients with significant renal (kidney) and/or hepatic (liver) disease, may require adjustment when starting/stoping cimetidine to maintain therapeutic blood levels.

In patients with poor liver143 or kidney function,144 as well as elderly patients at risk for neuropsychiatric illness,145 cimetidine dosage should be reduced to 300 mg every 12 hours, and further reduction may be necessary depending upon patient tolerability.

Close monitoring of prothrombin time (PT)146 is recommended with the anticoagulant warfarin (Coumadin®), and careful adjustment of the anticoagulant dose may be necessary with cimetidine treatment.

Aging men with pre-existing erectile dysfunction using sildenafil (Viagra®) should be aware that cimetidine boosts drug exposure by almost 60%,147 so men should strongly consider using a reduced dose of sildenafil (Viagra®) if concomitantly using cimetidine.

Sexual Side Effects In Men

Starting at the time of prescription use of cimetidine in the 1970s, multiple case reports began to appear in the peer-reviewed literature concerning sexual side effects, including loss of libido and erectile dysfunction.148,149 In addition, many reports of breast tenderness and tissue growth in men, known as gynecomastia,150 were published.151,152 Conservative post-marketing surveillance data suggests that the incidence of gynecomastia may be as high as one out of every 25 male patients treated with cimetidine for high stomach acid.153

These sexual side effects are not surprising since cimetidine is known to interfere with sex hormone binding sites in androgen responsive tissues,154 as well as increase prolactin levels and interfere with the peripheral activity of sex hormones like dihydrotestosterone (DHT).155

Since the risks for male sexual side effects and gynecomastia appear to increase with cimetidine dosages of 1,000 mg daily in men over the age of 40 years (though some men may experience sexual dysfunction within a short time of starting cimetidine at lower doses),149,152 older men should avoid doses of cimetidine in excess of 800 mg daily and treatment regimens longer than 60 days.
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Few nutritional sources have gained as much scientific validation as pomegranate. The vast majority of research has focused on extracts from the fruit. Only recently have scientists identified the synergistic action of compounds specific to other parts of the pomegranate—most notably its seeds and flowers.

The Next-Generation Pomegranate Formula

Life Extension® offers an advanced, cutting-edge pomegranate formula that brings together novel phytonutrients in a unique, high-potency blend.

Full-Spectrum Pomegranate™ combines standardized extracts from the whole fruit and flower, along with pomegranate seed oil, to support system-wide health. In addition to the highly absorbable antioxidant powerhouses found in pomegranate fruit, Full-Spectrum Pomegranate™ augments these polyphenols with newly discovered biologically active compounds from other parts of the pomegranate plant.

These little-known nutrients include: punicanolic acid that provides cellular support to help with inflammation, and pomegranate, to combat age-related metabolic changes.

This superior formula supplies the complete nutritional profile of the pomegranate plant. Just one softgel of Full-Spectrum Pomegranate™ provides polyphenols equivalent to 12.3 ounces of pomegranate juice concentrate (or 30 pomegranates) plus a proprietary blend of seed oil and flower extract.

POMELLA® extract is covered under U.S. Patent 7,638,640 and POMELLA® is a registered trademark of Verdure Science, Inc.

References
Dual-Action Support For Aging Joints!

As you grow older, age-related stiffness and discomfort in the joints becomes a fact of life. Activities once routine become a challenge as limited mobility hampers your every move.

You now have a more potent option to provide broad-spectrum support for aging joints. ArthroMax® Advanced with UC-II® and AprèsFlex® is a multi-nutrient formula based on scientific data on natural support for joint health. The ArthroMax® formula provides more joint support than ever before, enhanced with two innovative, clinically validated ingredients: AprèsFlex® and UC-II®.

Better Absorption For Optimum Benefit

AprèsFlex® represents a quantum leap forward in the delivery to aging joints of boswellia, long prized for its ability to help with inflammatory issues. It is a superior inhibitor of the enzyme 5-LOX (5-lipoxygenase) or 5-LOX.

Excess activity of 5-LOX results in the accumulation of leukotriene B4, a pro-inflammatory compound that affects aging joints. Boswellia has been shown to bind directly to the 5-LOX enzyme in our bodies, blocking it from facilitating production of pro-inflammatory leukotrienes.1,2

AprèsFlex™ boswellia absorbs into the blood 52% better than previously available forms of boswellia, for superior effectiveness.

ArthroMax® Advanced With UC-II® And AprèsFlex®

In addition to AprèsFlex®, ArthroMax® contains a novel form of standardized chicken cartilage: UC-II®. Data show it helps with immune issues that can impact joint discomfort and ease of motion in aging individuals.

Two capsules of ArthroMax® Advanced with UC-II® and AprèsFlex® provide the following nutrients in one convenient, joint-protecting formula:

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Amount</th>
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<tr>
<td>UC-II® standardized chicken cartilage</td>
<td>40 mg</td>
</tr>
<tr>
<td>Glucosamine sulfate 2KCl (from corn)</td>
<td>1500 mg</td>
</tr>
<tr>
<td>AprèsFlex® Indian frankincense (Boswellia serrata) extract</td>
<td>100 mg</td>
</tr>
<tr>
<td>Boron (calcium fructoborate as patented FruiteX B® OsteoBoron®)</td>
<td>1.5 mg</td>
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The retail price of a bottle of 60 capsules of ArthroMax® Advanced with UC-II® and AprèsFlex® is $36. If a member buys four bottles during Super Sale, the price is reduced to $21.60 per bottle.

References

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.
BOOST YOUR IMMUNE SYSTEM
It is rare for young people to develop cancer, life-threatening infections, or chronic inflammation. Why? Their immune systems are operating at peak capacity, turning “on” and “off” at precise times to eradicate pathogens, while not causing the chronic inflammation that can lead to cardiovascular disease and diabetes.

As we age, this picture of health changes rapidly. By then, we have depleted our valuable treasure chest of defensive immunity cells and the balance shifts to a less vigorous immune system.

Serious infections, cancers, and inflammatory diseases are among the leading causes of premature death in older adults. These disorders all arise from a common cause: the aging of the immune system, or immune senescence.

Immune senescence is now recognized as a major public health threat to aging populations.
Doctors today respond to *immune senescence* by treating each disease or condition separately,\(^{15-17}\) This approach fails to correct a major underlying mechanism behind both disease and aging and leaves us waiting for the next health problem to manifest.

After researching the causes of immune senescence, scientists have identified two botanicals that can provide powerful, complementary restorative properties that strengthen the two main branches of the immune system through unique mechanisms.

*Cistanche* primarily targets the *adaptive* immune system,\(^{18}\) the specialized branch of the system that allows for a stronger immune response tailored to specific pathogens while providing longer-lasting protection.

And the medicinal mushroom *Ganoderma lucidum*, or *Reishi*, has potent strengthening effects mainly on the *innate* immune system,\(^{19}\) the first-line component of the immune system that attacks foreign pathogens, including bacterial organisms, cells infected with viruses, and those transformed into malignant cells.\(^{20}\)

Aging individuals need robust function of both *adaptive* and *innate* immunity to remain protected against infections, cancers, and inflammatory diseases,\(^{21-25}\) Together, these bioactive agents, *cistanche* and *Reishi*, work in a complementary fashion to rejuvenate both major arms of the aging immune system.

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**Understanding Your Immune System**

Let’s take a quick tour of your immune system so that you understand how to best restore it to optimal functioning.

There are two main components of immune function that are intimately interconnected and work together to deliver round-the-clock surveillance and defense against body invasion.

*Immune senescence* involves the gradual loss of function of both of these components called the (1) *innate* and the (2) *adaptive* branches.\(^{26,27}\) Normally, both branches of the immune system work closely together, with the innate immune system taking the initial lead in defending the body against infection.\(^{28}\)

1) **Innate** immunity is the first line of defense to neutralize a foreign threat in the form of a bacterium, a virally infected cell, or a cell that has undergone malignant transformation early in the development of a cancer.\(^{29,30}\)

While the *innate* immune system is launching its first attacks, the *adaptive* immune system starts to ramp up its targeted defenses that include "smart" weapons like antibodies against specific organisms and the group of immune system cells known as *T-cells*.\(^{31,32}\)

2) **Adaptive immunity**, with its heavy reliance on T-cells, begins to fade surprisingly early in life. The primary source of T-cells, the thymus gland in the chest, begins to shrink by young adulthood, making new, naïve T-cells increasingly rare.\(^{11,33-35}\)
The Importance Of T-Cells

T-cells can be considered the “brains” of the immune system. The immune system includes two types of T-cells: naïve T-cells and memory T-cells. These two types of T-cells allow the body to produce specific responses to new and repeating threats. Without T-cells, any minor infection such as a cold or a minor cut could ultimately result in death.

Naïve T-cells, which are abundant in our young life, respond to new threats that occur to the body. However, once they have responded to a specific virus or bacteria, they “learn” the molecular pattern of this threat and convert to memory T-cells. These memory T-cells are like a stored number on your cell phone; they are programmed to respond to a specific threat that has previously invaded the body. These memory T-cells are now programmed to respond to known threats, but will not rally to head off a new, unknown threat.

So, for example, if you catch the flu as a child, your body will send out a fleet of naïve T-cells to attack and mop up the infection. As an adult, if you are exposed to a similar flu virus again, your body will send out a fleet of memory T-cells to prevent the infection.

As we age, we build up an increasing inventory of memory T-cells that have “memories” of previous infections, which allows them to respond quickly to a similar invasion.

Unfortunately, as we build up this inventory of memory T-cells, we also deplete our inventory of naïve T-cells. This depletion can have tragic results as we age. With fewer naïve T-cells to respond to new attackers, the body can become vulnerable and quickly devastated. The body will increasingly respond only to “known and repeated” threats and overlook “new” threats.

It seems with each passing day there are new threats emerging, such as new strains of flu or nascent cancer cells for which we must be prepared.

Fortunately, two botanicals, Cistanche and Reishi, can provide a powerful, natural means of boosting both adaptive and innate immunity. Each of these bioactives works in a unique and complementary fashion to stimulate the two key factors in a waning immune system.

Boost The Immune System To Increase Life Span

• Immune senescence, or aging of the immune system, is a key underlying cause of symptoms of aging, such as influenza, pneumonia, and a host of viral, bacterial, and fungal diseases.

• Reduced function of your immune system also predisposes you to cancer and autoimmune disorders, both of which require functioning immunity to keep at bay.

• Taken together, the results of immune senescence contribute to exaggerated rates of early death.

• You can fight the impact of immune senescence in your own body by addressing the two major divisions of the immune system.

• Extracts of Reishi primarily restore vigor and normal function to the innate branch of the immune system, the inborn system responsible for the immediate, nonspecific responses to threats that allow your body to fend off previously unseen organisms and abnormal cells.

• Extracts of the herb Cistanche primarily boost the highly modulated adaptive branch of the immune system responsible for longer-term, more specific responses to threats and provide swift responses when you are re-exposed to a threat your body has “seen” previously.

• Both of these natural supplements have been shown to prolong life in animal studies, and both produce immune-boosting functions in human trials.

• Both innate and adaptive immunity can be strengthened with this combination of healing herbs, now shown to have effects demonstrable by modern immunological assays.
Cistanche: Support For Adaptive Immunity

Extracts of the Cistanche plant species have been used for thousands of years as a tonic for a variety of age-related disorders. In Traditional Chinese Medicine, Cistanche is used for its perceived ability to promote immune function in older people, which is now being proven by today’s scientific understanding of immune senescence.

Cistanche extracts have broad-spectrum benefits for the immune system, with the bulk of their effects producing favorable changes in age-related adaptive immunity.

Chronic Viral Infection Worsens Immune Senescence

An important but little-regarded viral infection has now been found to contribute to accelerated immune senescence in a large number of aging adults. Cytomegalovirus, or CMV, is a member of the herpesvirus family that embeds itself in T-cells, where like a computer virus, it “runs in the background,” using up cellular resources while weakening the effectiveness of the immune system as a whole.

Older adults who test positive for CMV in their blood have a significantly higher immune risk profile than do uninfected people, which puts them at increased risk of early death related to immune senescence. Studies reveal that chronic CMV infection, which typically produces no detectable symptoms, is strongly associated with an accumulation of weakened memory T-cells, and a concomitant reduction in the naïve T-cells necessary to cope with new infectious or malignant threats.

And CMV-infected people die earlier: One study found a 42% increase in the annual death rate among older adults with CMV compared to those without, corresponding to a 3.7-year reduction in life expectancy after age 65. Conversely, members of very long-lived families appear to have better control of the virus and these people, even when CMV infected, have fewer of the T-cell abnormalities associated with immune senescence, and thereby live longer.

While there is little you can do to prevent or directly treat CMV infection, you can fight its deleterious effects on your longevity by doing all you can to boost your adaptive and innate immune systems using natural supplements such as Reishi and Cistanche extracts (and if need be customized prescription drug regimens).

One of the major components found in Cistanche species is echinacoside, which stimulates the creation of T-cells and enhances cell survival by reducing apoptosis.

Echinacoside increases the expression of a vital growth factor that benefits immune function by potentially suppressing the premature conversion of naïve T-cells into activated memory T-cells. This is important because as we age, our naïve T-cells dwindle in numbers, which reduces our protective immune function.

But now there is a way to help increase the dwindling pool of naïve T-cells needed for later responses to new threats, Cistanche raises levels of a growth factor that not only promotes increases in naïve T-cells, but has also been studied as a novel approach to minimizing the autoimmune response so common in immune senescence.

As we age, our immune systems are less able to properly control inflammatory responses. Normally, our regulatory immune cells shut down inflammation at an appropriate time. With the onset of immune senescence, these regulatory cells lose their potency and tissues normally protected against inflammation become vulnerable to an ongoing attack by inflammatory cells. This component of immune senescence is responsible for persistent inflammation in autoimmune diseases such as lupus (where connective tissue is attacked), rheumatoid arthritis (where joint lining tissue is attacked), and inflammatory bowel diseases (where intestinal lining tissue is attacked).

Increased Life Span With Cistanche

One of the most comprehensive and exciting outcomes of recent Cistanche research has been in the promotion of longevity. These studies indicate that enhancing immune function in older organisms prolongs life span.

A recent study looked at the use of Cistanche extracts as a way to delay aging. In the study, mice were given four weeks of supplementation with Cistanche extracts containing 8.25% by weight echinacoside. The scientists found that Cistanche extracts extended life span. The subjects of this study were a special strain of “senescence-accelerated mice,” which age at a much faster rate than do normal mice, making them ideal for aging studies.

The control mice that were not treated with Cistanche extracts survived up to 385 days. In the treated group, 40% of the Cistanche-supplemented animals remained alive! The untreated control mice had an average life span of 325 days, which is significantly shorter than the Cistanche group (375 days).
Reishi mushrooms (Ganoderma lucidum) are well known in Asian traditional medicine, with multiple uses for promotion of health and longevity.\textsuperscript{54,55} Working in a way that is complementary to Cistanche, Reishi extracts enhance the innate immune system, boosting the function of its components to prevent premature aging and death.\textsuperscript{56}

This was shown dramatically in a study of healthy adult mice.\textsuperscript{56} At the age of one year (which is middle age for a mouse), the animals were fed either control chow without supplementation, or chow enriched with Reishi extracts. By 88 weeks of life (old age), the average age of survivors (when half the animals in each group had died) was up to 66 days longer in Reishi-supplemented mice than in control animals. At the point when only 20\% of mice survived, the Reishi-supplemented mice were up to 110 days older on average than were control mice, while by the time only 10\% survived, the remaining Reishi-supplemented animals were up to 148 days older or more than controls.

The reasons for this longevity factor became apparent as researchers examined the immune cells. The control mice who did not take Cistanche extracts had an abundance of poorly functioning memory T-cells, like most aging humans. The mice also had low numbers of naïve T-cells.

The Cistanche-supplemented animals that were on a low-dose human equivalent to 210 mg/day had increases in naïve T-cells and had lower populations of memory T-cells, which is similar to a youthful immune system that is highly functional. What the study tells us is that the mice given Cistanche extracts had more immunological reserve and potentially were better “primed” for dealing with new threats to their longevity.

This study also provided evidence that Cistanche extracts have beneficial effects on innate immunity as well, by boosting levels of natural killer (NK) cells and reducing levels of the pro-inflammatory cytokine interleukin-6 (IL-6).\textsuperscript{18}

We can now connect the dots between animal and human studies with Cistanche.

Protecting Human Immunity

In a study from Japan, healthy older men and women (aged 65 to 80 years) were supplemented for 12 weeks with Cistanche extracts (containing 8.5\% by weight echinacoside) in a nutritional formulation.\textsuperscript{53} Scientists found impressive gains in immune factors after supplementation. Subjects in this study had significant increases of 11.7\% in natural killer (NK) cell activity (components of innate immunity), which offer protection against new invaders. The researchers also showed a 20.2\% increase in the ratio of beneficial CD4 T-cells to CD8 T-cells. An increased CD4/CD8 ratio is indicative of healthy, youthful immune function.

This human study, taken together with the previous animal studies, provides a link between enhanced immunity and longevity. It can be assumed that boosting adaptive immunity with Cistanche extracts may assist in prolonging human life span.

Reishi Extract: Enhancing Innate Immunity

Boosting adaptive immunity is only half of the story in managing immune senescence. To have a successful immune system, you also need an active innate immune response in order to fully identify and destroy threats from infections, malignancies, and out-of-control inflammation. Remember, without a strong, nonspecific innate immune response, your body won’t have time to develop the adaptive immunity you need to survive new threats.

Using Immune-Boosting Supplements

Boosting your immune function by enhancing both innate and adaptive immunity is clearly beneficial. Comprehensive support for both adaptive and innate immunity may be achieved with the use of standardized Cistanche and Reishi extracts all year-round.
In other words, it took significantly longer for the Reishi-supplemented mice to be negatively impacted by the effects of aging. The bottom line is that the surviving mice who took Reishi were older than their unsupplemented peers.

Reishi’s life-extending effects on boosting immunity include enhancements to:57-59

- Cytotoxic T-cells that attack and kill aberrant cells that can’t provide proper identification as part of one’s “self”, such as virus-infected cells or cells that may be turning malignant.
- Neutrophils, which blast invaders with destructive chemical bursts,
- Cytokines, signaling molecules that draw in attack cells,
- Toll-like receptors, which are molecular pattern-detection receptors on immune cells that identify dangerous molecular patterns carried by pathogens,
- Major histocompatibility (MHC) interactions that distinguish between human tissue types and foreign materials; their enhancement reduces malignant cells’ ability to hide from the immune system.60

Reishi extracts also reduce secretion of the pro-inflammatory cytokine IL-6; high levels of IL-6 in human populations is closely associated with shorter life spans.55,61,62

On the other hand, Reishi enhances production of interleukin-10 (IL-10), the cytokine associated with greater longevity in human studies.51,61,63 Additionally, Reishi regulates the innate immune response by suppressing TNF-alpha, which is a major pro-inflammatory signaling molecule.55,61

Reishi extracts have been shown to stimulate cell-killing activity by modulating dendritic cells, which is important since these cells help eradicate both virus infected and malignant cells.59 And polysaccharides from Reishi enhances two major features of innate immune system cells: phagocytosis (engulfing and destroying microorganisms) and chemotaxis (movement of attack cells towards a threatening invader).64

All of these innate immunity-boosting properties come to fruition in studies of Reishi as an antiviral agent. Polysaccharides from Reishi are especially effective against viruses in the herpesvirus family, which includes herpes simplex viruses responsible for oral/genital herpes and shingles, respectively.65,66 Another herpesvirus, cytomegalovirus, is responsible for many of the features of immune senescence that accelerate aging and reduce longevity.

Human studies are beginning to show potent antiviral activity against herpes simplex viruses. People infected with herpes zoster viruses may suffer from post-herpetic neuralgia, a severely painful nerve disorder that can linger for years as a result of the virus taking refuge in nerve cells. In an early proof-of-concept study, patients who did not respond to standard treatment, as well as those with painful shingles outbreaks, experienced dramatic reduction in pain using Reishi.67

In fact, Reishi extracts reduce viral, bacterial, and parasitic organisms sufficiently well and have been used as natural additives to the feed of a variety of animals and birds.68-71 In one study, extracts from the mushroom stimulated innate immunity by activating bacteria-engulfing cells called macrophages to devour the human pathogen Listeria monocytogenes.69

Summary

Aging of the immune system, or immune senescence, is a major component of systemic aging and a leading cause of life-shortening diseases of aging such as infectious diseases, malignancies, and chronic inflammatory disorders.

Immune senescence encompasses cumulative deficits in the innate, or first-line, branch of the immune system, which is why older adults respond poorly to vaccines and may experience recurrence of diseases that their bodies had previously encountered.

Two immune-boosting botanical extracts—from Cistanche herbs and from Reishi mushrooms—have now been shown to exert powerful and complementary effects on the innate and the adaptive immune systems. Both supplements increase longevity in animal studies, presumably related to the impact of Cistanche mainly on adaptive immunity and to Reishi’s impact mainly on innate immunity.

We can’t ignore the lethal impact that immune senescence inflicts on our aging bodies. Increased susceptibility to bacterial, viral, and fungal infections, to cancer development, and to autoimmune/inflammatory diseases are all manifestations of immune senescence. All can shorten our life spans.

Exciting studies of Cistanche and Reishi extracts show how they can help restore youthful immune function.

If you have any questions on the scientific content of this article, please call a Life Extension® Health Advisor at 1-866-864-3027.


31. Priest SO, Baumgarth N. The role of innate signals in B cell immunity to influenza virus. Front Biosci (Schol Ed). 2013;5:105-17.
All brains decline with age, but numerous studies show that the proper nutrients can promote more youthful cognition and enhanced memory.

Only Cognitex® combines 11 essential ingredients in one cost-effective formula.

Sold separately, these components sell for a small fortune in Europe, where they are commonly prescribed for optimal brain health. The following is a sample of what you’ll find in each softgel:

- **Alpha-Glyceryl Phosphoryl Choline**: boosts levels of acetylcholine, which enables brain cells to communicate.
- **Gastrodin**: a brain shield that supports healthy levels of blood flow.
- **Grape Seed Extract**: boosts brain oxygen flow.
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Cognitex® with Pregnenolone & Brain Shield® is the most advanced neuro-enhancing formula on the market.

The retail price for 90 softgels of Cognitex® with Pregnenolone & Brain Shield® is $90. If a member buys four bottles during Super Sale, the price is reduced to $55.75. If eight bottles are purchased during Super Sale, the price is reduced to $33.75.

Cognitex® is also available without pregnenolone at a slightly lower cost. Item #01896

To order Cognitex® with Pregnenolone & Brain Shield®, call 1-800-544-4440 or visit www.LifeExtension.com

These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.
Cistanche Rejuvenates Aging Immune System

Scientists have discovered that the echinacoside compound found in Cistanche plant extract stimulates the development of naïve T-cells and leads to a lower amount of memory T-cells, thereby creating a more balanced immune response. Cistanche also increases Natural Killer (NK) cell activity—resulting in a 15% lifespan increase in animal research!¹

A 12-week human study of a dietary supplement containing standardized Cistanche, resulted in impressive gains in immune factors after supplementation. Subjects had significant improvements, including an 11.7% increase in natural killer (NK) cell activity and a 20.2% improvement in the ratio of CD4 to CD8 cells. An increased CD4/CD8 ratio is indicative of healthy, youthful immune function.²

Reishi Mushroom Combats Immune Senescence

The numerous bioactive components of the Reishi mushroom exert powerful effects that may reverse many of the factors of immune senescence.³

Reishi extracts boost the function of innate immune cells, the immune system’s first line of defense.⁴⁻⁵

It has long been known that Reishi’s unique polysaccharides, triterpenes, and other constituents⁶ enhance the body’s hematopoietic stem cells, macrophages, and other crucial immune factors.⁷⁻⁸ Animal research shows Reishi supports multiple aspects of immune function and longevity.⁹

These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.
Ultra-Potent, Dual-Extract Formulation

Now, both Cistanche and Reishi are available in one powerful, dual-extract formulation, specifically created for year-round support of the aging immune system!

Immune Senescence Protection Formula™ with standardized Cistanche and Reishi is our maximum dual-extract defense against immune senescence.

The suggested serving of two vegetarian capsules daily of Immune Senescence Protection Formula™ provides:

Cistanche tubulosa extract (stem and leaf) 210 mg
[std. to 22% echinacosides (46.2 mg)]

Reishi mushroom (Ganoderma lucidum) extract 980 mg
(Fruit body) [std to 13.5% polysaccharides (132.3 mg)
and 6% triterpenes (58.8 mg)]

Reishi mushroom (Ganoderma lucidum) spore 150 mg

A bottle of 60 vegetarian capsules of Life Extension® Immune Senescence Protection Formula™ retails for $40. If a member buys four bottles during Super Sale, the price is reduced to $24.30 per bottle.

Standardized Cistanche

For those seeking the effects of Cistanche only, Life Extension® has created a standalone Standardized Cistanche that contains the same echinacosides as in the Immune Senescence Protection Formula™. For a very low price, a member can obtain the recommended 210 mg daily Cistanche dosage in a single, high-potency capsule providing a potent 46.2 mg dose of echinacosides.

Standardized Cistanche provides powerful support against immune senescence.

The suggested dosage of one vegetarian capsule of Standardized Cistanche provides:

Cistanche tubulosa extract (stem and leaf) 210 mg
[std. to 22% echinacosides (46.2 mg)]

Vitamin C (as ascorbyl palmitate) 2 mg

A bottle of 30 vegetarian capsules of Life Extension® Standardized Cistanche retails for $20. If a member buys four bottles during Super Sale, the price is reduced to $10.80 per bottle.

To order Life Extension® Immune Senescence Protection Formula™, or Standardized Cistanche call 1-800-544-4440 or visit www.LifeExtension.com

References
ACTIVATE YOUR
NATURAL KILLER CELLS

To Guard Against Infection And Malignancy

Flu viruses are responsible for as many as 50,000 deaths every year in the US.¹
Bacterial pneumonia² causes over 60,000 deaths annually.³⁴
Annual flu and pneumonia vaccines are common, but they might not be sufficient to fight off wintertime infections in the presence of a weakened immune system known as immune senescence.⁵⁻⁸

The first line of defense against new invaders is our natural killer (NK) cells. As we age, NK cells lose their functionality, thus leaving us far more vulnerable to viral diseases—and the formation of tumors.⁹,¹⁰

Aging humans don’t have to succumb to this massive loss of NK cell function. Scientists have uncovered an enzymatically modified rice bran that has been shown to increase NK cell activity in circulating blood cells by up to 84%!¹¹

By optimizing your NK cell function, you will be raising defenses against early death from viral illness—and against cancer as well. Enzymatically modified rice bran has been proven to help restore NK cell activity and may thereby shorten the duration and severity of winter illnesses.¹²
ACTIVATE YOUR NATURAL KILLER CELLS TO GUARD AGAINST INFECTION AND MALIGNANCY

Powerful Immune Defense

Natural killer cells (NK cells) are one of your body’s most powerful defenses against infections and cancer.13-15 These tiny security guards seek and destroy cells that have been transformed by an infection with a virus or one of many malignant changes that transform them into cancer cells.9,16

NK cells work by triggering apoptosis (programmed cell death) in cells that have been transformed by a virus or malignancy.17,18 Without this critical defense mechanism, viruses can be spread throughout the body and cancer cells can form invading, metastasized tumors.9,19

The health of these cells is critical to a robust immune system. Unfortunately, your NK cell function rapidly declines as part of the natural decline in your immune system as you age.20-22 This degeneration of immune function is medically termed immune senescence.

This explains, in part, why aging individuals become such a ready target of each year’s new influenza outbreak despite being vaccinated against the flu. Anywhere between 5 to 20% of the US population gets the flu every year, in a seasonal wave that begins as early as October, often peaks in February, and can last until May.23-25 Older adults are at especially high risk: 90% of seasonal flu-related deaths, and up to 60% of flu-related hospitalizations, occur in people 65 and older,26 which happens to be the age when NK cell function precipitously declines.27,28 And the older we get, the higher the risk of a hospitalization or death from the flu.29

When you were younger, your NK cells, which are part of your innate immune system, could destroy the new strain of virus while your adaptive immune system “learned” its properties and then made antibodies to destroy any remaining virus.30-33 But because your NK cell function declines with age, you can easily be rapidly overwhelmed by new viral strains before your slower adaptive immunity can develop.

Similarly, older adults are at an increased risk of cancer because falling NK function fails to destroy malignant cells early on, allowing them time to develop various tricks that evade adaptive immunity while they grow into life-threatening tumors. Younger people have more robust NK function, which helps explain why cancers are generally so rare before late middle age.

Why Mainstream Medicine’s Solutions Don’t Work

Mainstream medicine has little to offer to counteract declining NK cell function. Although new vaccines can help protect against specific viruses, a decline in immune function (as part of immune senescence) limits vaccine efficacy in older people.34 More potent antiviral drugs can be developed—again to combat specific viruses—but the problem with these drugs is that they have substantial toxicity,35 they are given only after a viral infection has established itself, and they are extremely costly.36-39 Specific cytokine injections (such as low-dose interleukin-2) may help replace other components of waning immunity, but again, side effects and high costs limit their widespread use.40,41

A better approach would be to change the way the body responds to threats like viruses and tumor cells by directly boosting NK cell function and restoring waning immunity caused by immune senescence.5,43

By enhancing NK cell function, you would potentially be improving resistance, not to one or a few related viruses, but to virtually all viruses at once.44 In the process, you would also be potentially enhancing natural cancer resistance, not to specific cancer types, but to virtually all malignancies at once.45

Fortunately, as a result of years of research by immunologists, infectious disease experts, and oncologists, a natural compound has been discovered that can significantly improve declining NK cell function precisely when it is needed the most—during the vulnerable winter season when infectious flus are at their peak.
ACTIVATE YOUR NATURAL KILLER CELLS TO GUARD AGAINST INFECTION AND MALIGNANCY

What You Need To Know

Recently, there has been an explosion of interest in EMRB as an NK cell-boosting agent to overcome the reduction of NK cell activity due to immune senescence. Several basic laboratory and animal studies have helped to set the stage for EMRB’s effects on NK cell function.

**Seasonal Flu Defense**

- Immune senescence is the age-related dysregulation and steady loss of function of various components of the immune system; it explains the rise in infections, cancers, and even autoimmune problems seen in elderly populations.
- The reduction of one particular component of immunity—activity of natural killer cells—leaves older adults uniquely vulnerable to viral infections, especially during the wintertime peak in influenza.
- Natural killer (NK) cells are the body’s frontline security team, identifying and eliminating cells infected with viruses or transformed by cancer.
- A unique product, enzymatically modified rice bran (EMRB), has now been developed, EMRB boosts NK cell activity by nearly 84%.
- EMRB is also effective at reducing deaths from certain cancers, further testimony to its boost of NK function.
- The wintertime viral season is precisely the time that this product should be used for optimum protection.
- Support the rest of your immune system year-round with other supplements capable of fighting off immune senescence in all branches of your defenses, and use EMRB as your wintertime immune enhancer.

**EMRB Boosts NK Cell Activity In Just Two Days!**

An especially promising early animal study demonstrated the power of EMRB for boosting NK cell activity. When old mice with age-related reduction of NK function were injected with EMRB, they showed a greater than five-fold increase in NK cell activity within just two days of treatment. The enhanced NK activity in this study also resulted in increased binding of NK cells to target tissues and boosted the amounts of cell-killing chemicals inside each cell.

**Natural Compound Boosts NK Cell Function**

A derivative of rice bran called enzymatically modified rice bran (EMRB) has been shown to promote robust NK cell function in animal and human studies. By mechanisms that are still under investigation, EMRB has been shown to increase NK cell activity in circulating blood cells by up to 84%.

Arabinoxylan is a type of indigestible fiber found in cell walls of the hard components of plants, such as in the husks, or bran, of cereal grains. Enzymatically modified rice bran is produced by exposing crude fiber from rice bran to enzymes isolated from the Japanese culinary mushroom, shiitake (Lentinula edodes).
“Natural killer cells” are one of your body’s leading defenses against dying. That’s because these specialized immune cells are natural killers of cells that have become transformed, either by infection with a virus or by one of many malignant changes that mutate them into cancer cells.9,16

Natural killer (NK) cells are part of your innate immune system, that part of the immune system that was ready to go the moment you were born (innate means “from birth”).64 Unlike cells belonging to your adaptive immune system, NK cells don’t require specific antibodies to do their work.65

Rather, NK cells come fully equipped to recognize any cells that don’t belong in your body.65 Such cells include those whose replicative machinery has been taken over by a virus, and also cells that have gone rogue to replicate without natural controls, such as cancer cells.16

Thus, NK cells normally patrol throughout your body, acting almost like tiny but well-armed security guards. As they circulate in your bloodstream, NK cells constantly seek out cells that lack the proper “ID badge,” in the form of molecular patterns indicating that they are authorized parts of your biological self.66-69

Once such unauthorized cells have been identified, NK cells shoot to kill, destroying virally or malignantly transformed cells, while leaving intact any normal, healthy cells that can prove their identity.68 NK cells use as weapons chemical substances that punch holes in target cell membranes, allowing them to insert proteins that trigger the cell death program called apoptosis, which lies latent in every cell.70

Cells infected by viruses are detrimental to our body, both acutely and chronically. Destruction of virally infected cells by apoptosis prevents continued intracellular replication of viruses.16,70

Functional NK cells are needed to destroy virus-infected cells before viral replication gets out of control. Failure of NK cells to control an infection results in release of new viruses, followed by more rapid infection, viral replication, and destruction of millions of additional cells, spreading the virus throughout the body.

In the case of malignant cells, NK cell-induced apoptosis can stop a developing cancer in its tracks, preventing further replication of cells before they can form an invading, metastasizing tumor.71

NK cells have recently been found to have other important functions vital to infection- and cancer-free survival:

- NK cells secrete cytokines, which are chemical signaling molecules that regulate the activity of other immune system cells;5
- NK cells are essential to stopping inflammatory responses once they’ve done their work,72-74 for example, by deleting populations of senile immune cells. NK cells can shift the immune system’s focus away from a target that has already been neutralized;75
- NK cells can enhance the immune response to ongoing threats by stimulating “B-lymphocytes” to produce antibodies that destroy specific antigens.76

Unfortunately, a decline in NK cell function with age can leave older adults uniquely vulnerable to viral infections, especially during the wintertime peak in influenza. But a unique formula of enzymatically modified rice bran (EMRB) has been developed that has boosts NK cell activity by nearly 84%, potentially reducing the severity and duration of viral illnesses—and death from certain cancers as well.
Another important benefit derived from EMRB’s activation of NK cells is that it enhances the body’s immune response to vaccines against both infections and cancers. This is of special importance to older adults, whose vaccine responses are often weaker than desired. Finding effective ways to boost the vaccine’s efficacy is a major priority in adult vaccine development.

In a landmark study of cultured human blood cells, EMRB inhibited the replication of one of humanity’s most-feared viruses, HIV, by boosting multiple immune responses that are typically suppressed by the AIDS virus. A series of cell culture studies has also established that EMRB’s ability to activate NK cells helps fight cancer. One such study showed that EMRB increased susceptibility of both human and mouse breast cancer cells to a common chemotherapy drug by more than 100-fold. This has tremendous implications for reducing the doses of toxic chemotherapy agents in current use.

And in cells from human T-cell leukemia, EMRB alone induced the death of malignant cells.

Human Studies Prove EMRB’s Benefits

Human studies on supplementation with EMRB are equally impressive.

When a group of 20 healthy adult men and women were supplemented with EMRB for 60 days, with either a dose of 1,000 mg/day or 3,000 mg/day, NK cell activity in both groups jumped by approximately 35% in the first week. A similar effect was shown in another study when a lower dose of 500 mg/day of enzymatically modified rice bran was given to healthy subjects between 45 and 55 years old. With EMRB supplementation, all participants experienced a significant three-fold enhancement of NK activity in just three to four weeks—with no side effects.

In a four-month study in individuals who were initially low in NK cell activity, supplementation with 1,000 mg/day of EMRB led to a four-fold increase in NK cell activity at two months, compared to control responses. And at the end of four months, participants showed a seven-fold increase in NK cell activity.

EMRB has also been studied in human patients with malignancies with remarkable results. In 48 patients with multiple myeloma, a blood cancer, whose median age was 65 years, a dose of 2,000 mg/day for three months produced a significant near 84% increase in NK cell activity by the end of the second month of supplementation.

This increase in NK cell activity could potentially result in longer life spans, as demonstrated by the next study on patients with a deadly form of liver cancer called hepatocellular carcinoma. In a three year randomized, controlled trial of EMRB vs. placebo, supplemented patients had a reduced recurrence rate of the cancer (31.6% EMRB-group versus 46.7% in controls). Supplemented subjects also lived longer:

- At one year, 76% of supplemented subjects were alive, but only 63% of control patients survived;
- At two years, 35% of supplemented patients were alive, but only 6.7% of control subjects survived; and
- By two and a half years, 11% of supplemented subjects survived, while no control patient remained alive.
ACTIVATE YOUR NATURAL KILLER CELLS TO GUARD AGAINST INFECTION AND MALIGNANCY

Summary

At the peak of the wintertime virus season, older adults are uniquely vulnerable to potentially life-threatening infections. This is part of the bigger picture of immune senescence, the natural decline of our immune function with age.

NK cells normally provide your body’s first, immediate response to previously unknown threats. Since NK cell function declines with age, we should consider taking special steps during the winter season to fill in this critical component of immune function.

Studies show that enzymatically modified rice bran (EMRB) rapidly and significantly boosts aging NK activity, with real-world effects demonstrated on both viral infections and cases of malignancy. Maturing individuals should take steps to maintain and strengthen immune function year-round with supplements (such as Cistanche and Reishi) aimed at the innate and adaptive immune responses.

During the high-risk winter months, however, it would appear to be quite beneficial to add the NK cell activity-boosting effects of EMRB. This can provide the added protection needed to conquer acute and chronic issues that can markedly shorten life spans.

During that four-month period, you may also be ridding your body of accumulated precancerous cells and inflammation-generating senescent cells that have outlived their usefulness.

If you have any questions on the scientific content of this article, please call a Life Extension® Health Advisor at 1-866-864-3027.

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ACTIVATE YOUR NATURAL KILLER CELLS TO GUARD AGAINST INFECTION AND MALIGNANCY


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ACTIVATE YOUR NATURAL KILLER CELLS TO GUARD AGAINST INFECTION AND MALIGNANCY


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Aging is Characterized by Inflammation, Glycation, and Mitochondrial Decay

The loss of cellular vitality is caused by a number of factors, including mitochondrial problems, glycation, and free-radical reactions. Life Extension members have access to a state-of-the-art nutritional formula called MITOCONDRIAL ENERGY OPTIMIZER with BioPQQ® that helps protect delicate cellular structures and enables cells to perform lifelong-sustaining metabolic processes.

Mitochondrial Energy Optimizer with BioPQQ® is designed to counteract age-related structural and functional changes by providing the following unique ingredients:

- **CARNOSINE**: As humans age, proteins in their bodies become irreversibly damaged by glycation reactions. Glycation is the cross-linking of proteins and sugar to form non-functioning structures called advanced glycation end products in the body, which can lead to alterations of normal cell function. Carnosine is not only a powerful anti-glycating agent, but it also protects neurons against reactive and cytotoxic protein carbonyl species associated with normal aging.1,2

- **PQQ**: This breakthrough micronutrient has been shown to trigger mitochondrial biogenesis—the growth of new mitochondria in aging cells!3 PQQ also effectively modulates multiple destructive biochemical pathways that are induced by higher than desirable blood glucose levels. Human mortality studies indicate that fasting glucose levels are between 74–85 mg/dL. Yet many aging people have fasting glucose above 90 mg/dL, which is less than optimal.4-7 Benfotiamine protects endothelial cell integrity from glycation end products in the body, which can lead to alterations of normal cell function.5-8 Luteolin—a flavonoid that has been shown to help suppress pro-inflammatory cytokines—is less than optimal.9-12 Benfotiamine protects endothelial cell integrity from glycation end products in the body, which can lead to alterations of normal cell function.5-8 Luteolin—a flavonoid that has been shown to help suppress pro-inflammatory cytokines—is less than optimal.9-12

- **PYRIDOXAL 5’-PHOSPHATE**: Aging results in the formation of advanced glycation end products throughout the body. Pyridoxal 5’-phosphate is the active form of vitamin B6 that has been shown to protect against both lipid and protein glycation reactions.13-16

- **R-LIPOIC ACID**: Destructive free-radical activity in the mitochondria plays a major role in the loss of cellular vitality. A microencapsulated Bio-Enhanced® R-lipoic acid facilitates youthful mitochondrial energy output while guarding against free radicals. Two forms of lipoic acid are sold on the supplement market, but R-lipoic acid is far more potent.17-20

- **ACETYL-L-CARNITINE ARGINATE**: Effectively modulates multiple destructive biochemical pathways that are induced by higher than desirable blood glucose levels. Human mortality studies indicate that fasting glucose levels are between 74–85 mg/dL. Yet many aging people have fasting glucose above 90 mg/dL, which is less than optimal.1-5 Benfotiamine protects endothelial cell integrity from glycation end products in the body, which can lead to alterations of normal cell function.5-8 Luteolin—an antioxidant that has been shown to help suppress pro-inflammatory cytokines—is less than optimal.9-12 Benfotiamine protects endothelial cell integrity from glycation end products in the body, which can lead to alterations of normal cell function.5-8 Luteolin—an antioxidant that has been shown to help suppress pro-inflammatory cytokines—is less than optimal.9-12

Just four capsules of Mitochondrial Energy Optimizer with BioPQQ® provide:

- Carnosine 1000 mg
- ArginoCarn® Acetyl-L-carnitine arginate DiHCl 675 mg
- R-Lipoic acid (as microencapsulated Bio-Enhanced®) 150 mg
- Benfotiamine 150 mg
- Vitamin B6 (as pyridoxal 5’-phosphate) 100 mg
- BioPQQ® (Pyroloquinoline quinone disodium salt) 10 mg
- Luteolin 8 mg
- Calcium 230 mg

To order Mitochondrial Energy Optimizer with BioPQQ®, call 1-800-544-4440 or visit www.LifeExtension.com

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Bio-Enhanced® is a registered trademark of Genestra Research, Inc. ArginoCarn® is a registered trademark of Sigma-tau HealthSciences, and is manufactured exclusively under U.S. production patent 6,703,042 and worldwide production patent EP1202956. The combination of Acetyl-L-Carnitine and Alpha Lipoic Acid is patented by Sigma-tau under U.S. patent 8,345,822. BioPQQ® is a registered trademark of MGC (Japan).
Researchers are discovering how important probiotics are to overall health. Beyond improving digestive health, probiotics provide a broad spectrum of benefits throughout the body.

**FlorAssist® Heart Health Probiotic** contains a novel probiotic—*Lactobacillus reuteri* 30242—that has been shown in clinical trials to safely support healthy cholesterol in adults already within the normal range.¹,²

Additionally, *L. reuteri* 30242 has been shown to support healthy CRP (a marker for inflammation), fibrinogen (involved in clot formation), apoB-100 (a marker for LDL particle size, a known cardiovascular risk factor), and vitamin D levels (important for cardiovascular health) for those within normal range.³

**FlorAssist® Heart Health Probiotic** has been carefully formulated for convenient use as a safe, easy-to-swallow capsule with no unpleasant aftertaste. One capsule with food twice daily is the perfect addition to a heart-healthy lifestyle.

The suggested daily dose of two vegetarian capsules of FlorAssist® Heart Health Probiotic provides:

<table>
<thead>
<tr>
<th>FlorAssist®</th>
<th>5 Billion CFU*</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Lactobacillus reuteri</em> (NCIMB 30242)</td>
<td></td>
</tr>
</tbody>
</table>

* Colony Forming Units

A bottle of 60 vegetarian capsules of FlorAssist® Heart Health Probiotic retails for $32. If a member buys four bottles during **Super Sale**, the price is reduced to **$18.90** per bottle.

**References**

To order FlorAssist® Heart Health Probiotic, call 1-800-544-4440 or visit www.LifeExtension.com

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.
Natural killer (NK) cells function as the body’s first responders. As soon as NK cells sense a potential invasion, they are on the scene to initiate immune protection. Natural killer cells promote seasonal support for the body’s natural defense system.

In addition, functional NK cells recognize and eliminate senescent cells that accumulate in aged tissues and create metabolic disturbances.

As we age, natural killer cell activity markedly declines with an enzymatically concurrent weakening of normal immune functions.

For targeted seasonal protection, a formula called NK Cell Activator™ has been developed, which contains an enzymatically modified rice bran shown to be a potent immune modulator.

NK Cell Activator™ supports the activity of natural killer (NK) cells—crucial components of the innate immune system.

In one clinical study, scientists documented a 3-fold increase of natural killer cell activity in healthy individuals within three to four weeks of receiving 500 mg daily of the rice bran compound found in NK Cell Activator™.

In another double-blind, randomized, placebo-controlled study, researchers noted that subjects taking the enzymatically modified rice bran found in NK Cell Activator™ experienced a boost in myeloid dendritic cells—cells that act as key messengers between the innate and the adaptive immune systems.

A strategy to derive the unique functional effects of NK Cell Activator™ is to take one capsule daily for four months during the winter season.

The suggested single serving of one vegetarian tablet of NK Cell Activator™ provides:

| Proprietary Enzymatically Modified Rice Bran | 500 mg |

A bottle of 30 tablets of NK Cell Activator™ retails for $45. If a member buys four bottles during Super Sale, the price is reduced to $28.35 per bottle.
**Super Omega-3 EPA/DHA with Sesame Lignans & Olive Fruit Extract**
120 softgels, Item # 01482
Super purified EPA/DHA fish oil plus sesame lignans and potent olive (fruit and leaf) extract to provide critical omega-3 fatty acids and essential components of the Mediterranean diet.

**AMPK Activator • 90 vegetarian capsules, Item # 01907**
Activating AMPK “turns off” many of the destructive factors of aging, enabling cells to return to their youthful vitality. Research shows that the two plant extracts contained in this formula (Gynostemma pentaphyllum and trans-tiliroside), promote AMPK activation.

**Super Bio-Curcumin® • 400 mg, 60 vegetarian capsules, Item # 00407**
Super-absorbable formulation promotes healthy lipids, joint function, and healthy DNA. Absorbs up to seven times greater than conventional curcumin.

**NAD+ Cell Regenerator™ Nicotinamide Riboside**
100 mg, 30 vegetarian capsules, Item # 01904
Nicotinamide riboside is a revolutionary new form of vitamin B3 that is directly converted to NAD+, a coenzyme found in every cell that is essential for efficient energy transfer from food to energy.

**Super Booster with MacuGuard™ Ocular Support • 60 softgels, Item# 01980**
Just one softgel daily provides potent doses of vitamins K1/ K2, gamma tocopherol, sesame lignans, chlorophyllin, and lycopene, along with zeaxanthin, meso-zeaxanthin, lutein, and C3G for eye support.

**Two-Per-Day • 120 tablets Item # 01915**
Provides up to 50 times more potency of specific ingredients than commercial multivitamin/mineral formulas, along with unique ingredients not found in products like Centrum®. Also available in capsule form.

**Super Ubiquinol CoQ10 with Enhanced Mitochondrial Support™**
100 mg, 60 softgels, Item # 01426
The superior ubiquinol form of CoQ10 plus a natural compound (shilajit) shown to double mitochondrial CoQ10 levels.

**Life Extension Mix™ • 315 Tablets, Item # 01955**
This high potency multi-nutrient formula now includes a small dose of nicotinamide riboside, a revolutionary form of vitamin B3 that converts to a coenzyme in the body called NAD+, which is essential in “turning off” genes that promote aging.

**Vitamin D3 • 5,000 IU, 60 softgels, Item # 01713**
High-potency vitamin D in a softgel to provide greater absorption into the bloodstream.

**Ultra Natural Prostate • 60 softgels, Item # 01898**
Comprehensive support for an aging prostate gland utilizing standardized lignans, plus boron, and phospholipids for enhanced absorption.

**MacuGuard™ Ocular Support • 60 softgels, Item # 01885**
Offers triple eye protection with phospholipids, lutein, and zeaxanthins. This product is no longer needed for most people taking the new Super Booster that now contains these same ingredients.

**Super K with Advanced K2 Complex • 90 softgels, Item # 01724**
More potent formula includes 200 mcg of long-acting MK-7 form of vitamin K2, plus 1,000 mcg of K1 and 1,000 mcg of the MK-4 form of vitamin K2.

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These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.
<table>
<thead>
<tr>
<th>Product Description</th>
<th>Retail Price</th>
<th>Discount Price Per Bottle</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PQQ Caps with BioPQQ</strong>® • 10 mg, 30 vegetarian capsules, Item # 01500</td>
<td>$24</td>
<td>$14.85</td>
</tr>
<tr>
<td>Promotes mitochondrial biogenesis (generation of new mitochondria) in aging cells.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>DHEA (Dehydroepiandrosterone)</strong> • 25 mg, 100 capsules, Item # 00335</td>
<td>$18</td>
<td>$10.13</td>
</tr>
<tr>
<td>A hormone that declines with aging, benefits overall health.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mitochondrial Energy Optimizer with BioPQQ</strong>® • 120 capsules, Item # 01768</td>
<td>$94</td>
<td>$56.70</td>
</tr>
<tr>
<td>To maintain healthy cellular function, protein structural integrity, and mitochondrial biogenesis.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mega Green Tea Extract</strong> 725 mg, 100 lightly caffeinated vegetarian capsules, Item # 00953</td>
<td>$30</td>
<td>$16.20</td>
</tr>
<tr>
<td>A highly concentrated 98% polyphenol extract delivering 45% of the health-promoting catechin EGCG.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Optimized Resveratrol with NAD+ Cell Regenerator™</strong> • 60 vegetarian capsules, Item # 01930</td>
<td>$42</td>
<td>$24.30</td>
</tr>
<tr>
<td>Best-selling trans-resveratrol formula now contains nicotinamide riboside, a novel form of vitamin B3 that supports mitochondrial health, along with pterostilbene and fisetin, which work in synergy with resveratrol to “turn on” longevity genes.</td>
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</tr>
<tr>
<td><strong>Bone Restore with Vitamin K2</strong> • 120 capsules, Item # 01727</td>
<td>$24</td>
<td>$14.85</td>
</tr>
<tr>
<td>Highly absorbable forms of calcium and FruiteX B® OsteoBoron®, magnesium, zinc, and K2 as MK-7. Available with or without vitamin K2.</td>
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<tr>
<td><strong>Cognitex® with Brain Shield®</strong> • 90 softgels, Item # 01896</td>
<td>$60</td>
<td>$35.10</td>
</tr>
<tr>
<td>Optimal support for the brain. Includes gastrodin, glyceryl phosphoryl choline, vinpocetine, phosphatidylserine, uridine 5'-monophosphate, and more. Available with or without pregnenolone.</td>
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<tr>
<td><strong>Brain Shield® Gastrodin</strong> • 300 mg, 60 vegetarian capsules, Item# 01802</td>
<td>$33</td>
<td>$20.25</td>
</tr>
<tr>
<td>A unique compound providing unparalleled, multifactorial support for cognitive and circulatory brain function.</td>
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<tr>
<td><strong>ImmuneSenescence Protection Formula</strong> • 60 vegetarian capsules, Item # 01905</td>
<td>$40</td>
<td>$24.30</td>
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<tr>
<td>Standardized full-spectrum Reishi mushroom extract with Cistanche extract to regulate the immune system and restore youthful immune balance.</td>
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<td></td>
</tr>
<tr>
<td><strong>Triple Action Cruciferous Vegetable Extract</strong> • 60 vegetarian capsules, Item # 01468</td>
<td>$24</td>
<td>$14.85</td>
</tr>
<tr>
<td>Comprehensive cruciferous plant extract formulation, with 13C, DIM, apigenin, and other DNA-protecting vegetable concentrates.</td>
<td></td>
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<tr>
<td><strong>European Milk Thistle</strong> • 60 softgels, Item # 01822</td>
<td>$28</td>
<td>$16.88</td>
</tr>
<tr>
<td>High-absorption phospholipid-enhanced formula delivers nearly five times more active components to the bloodstream to support detoxification processes as well as promote liver health and function.</td>
<td></td>
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</tr>
<tr>
<td><strong>Skin Restoring Phytoceramides</strong> • 350 mg, 30 vegetarian capsules, Item # 01596</td>
<td>$25</td>
<td>$15.53</td>
</tr>
<tr>
<td>Oral phytoceramides derived from wheat can reach the skin’s deepest layers to offset the body’s natural decline with age.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ArthroMax® Advanced with UC-II® and AprèsFlex®</strong> • 60 capsules, Item # 01618</td>
<td>$36</td>
<td>$21.60</td>
</tr>
<tr>
<td>Promotes joint health and may promote comfortable joint structure and function.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>FlorAssist® Heart Health Probiotic</strong> • 60 liquid vegetarian capsules, Item # 01821</td>
<td>$32</td>
<td>$18.90</td>
</tr>
<tr>
<td>Contains a novel probiotic—L. reuteri 30242—shown to support healthy cholesterol in the normal range.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Advanced Bio-Curcumin® with Ginger and Tumarones</strong> • 30 softgels, Item # 01808</td>
<td>$30</td>
<td>$18.23</td>
</tr>
<tr>
<td>Triple-action formula acting on multiple signaling pathways to deliver broad-spectrum protection against inflammation.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Neuro-Mag™ Magnesium L-Threonate</strong> • 90 vegetarian capsules Item# 01603</td>
<td>$40</td>
<td>$24.30</td>
</tr>
<tr>
<td>Optimal form of magnesium to protect synaptic density of neurons.</td>
<td></td>
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</table>

Order online at www.LifeExtension.com/SuperSale

These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.
NR BOOSTS NAD+
Normal aging is accompanied by a noticeable increase in both mental and physical fatigue, along with a loss of motivation. The tiredness we outwardly feel reflects inward impairment of cellular functions critical to sustaining life.

This is in part the result of reduced levels of a compound called NAD+, found in every cell in the body and essential to life. NAD+ enables the transfer of energy from the foods we eat to vital cell functions and is required to turn “off” genes that accelerate degenerative aging processes.

Published research confirms that NAD+ levels decline as we age and represent a fundamental, systemic contributor of aging.

Finding a way to boost NAD+ levels, therefore, could help promote youthful vitality and even extend life span.

For the past 13 years, we at Life Extension have been searching for an efficient way for aging humans to affordably boost their cellular NAD+ levels. We came close in 2001, when one of our researchers developed an effective NAD+ boosting sublingual lozenge; unfortunately, it only maintained stability for a short time period.

Now, after more than a decade of searching, an effective NAD+ cell-boosting technology has finally become available.
As NAD+ levels decline, mitochondrial function is impaired, which results in fewer mitochondria surviving, and ultimately may lead to many of the physical symptoms of aging. Fortunately, by increasing intracellular NAD+ levels, age-related mitochondrial dysfunction can be reversed.9

2. Second, NAD+ activates3 key anti-aging enzymes called sirtuins.9,17,18 Sirtuins, specifically SIRT1 and SIRT3, are intimately related to longevity through their control of gene expression and require NAD+ for their activity.3,5,19,20-22 By activating these sirtuins, we’re able to gain control over one of our body’s anti-aging “switches.” SIRT enzymes “turn off” certain genes that promote aging, such as those involved in inflammation,23,24 in fat synthesis and storage,25,26 and in blood sugar management.25,26

Consequences Of Falling NAD+ Levels
The age-related decrease in NAD+ causes defects in both energy- and gene-related functions to accumulate. These defects feed on one another to produce the disorders we typically identify as aging.19 The consequences of a decline in NAD+ levels and subsequent reduction in SIRT1 and SIRT3 enzymes include:

- **Neurodegeneration** in the brain,19,27,28
- **Vascular inflammation**, producing damage to heart and blood vessels that can result in stroke or heart attack,29,31
- **Increased fat storage** in the liver, which could lead to nonalcoholic fatty liver disease (NAFLD),32-34
- **Increased fat production and deposition** in white adipose tissue (the primary fat storage form found in dangerous belly fat),35,36
- **Growing insulin resistance**, and
- **Fatigue, loss of muscle strength and decreased fatty acid oxidation**.39,40

To avoid these degenerative processes, it is essential that steps be taken to optimize the amount of NAD+ in our bodies.
A Natural NAD+ Booster

Nicotinamide riboside has been scientifically proven to maintain robust levels of NAD+ in cells, thereby both supporting vital cellular energy functions and activating the anti-aging enzymes SIRT1 and SIRT3. As a result, NAD+ provides an extraordinary range of longevity benefits that add up to a system-wide slowing and reversal of certain aging processes. In addition, nicotinamide riboside accomplishes this NAD+ boosting effect without the irritating skin flushing and rash caused by the standard forms of vitamin B3.

Directly boosting NAD+ with nicotinamide riboside presents a new and effective strategy for preventing the natural decline in cellular energy as we age by promoting youthful vitality.

Initial Studies On Nicotinamide Riboside

Nicotinamide riboside works through multiple mechanisms to promote life extension. Most dramatic are its effects on longevity and metabolism, as shown by recent laboratory studies.

In their early investigations into the effects of nicotinamide riboside on life span, scientists used a strain of yeast known to have a relatively short average life span of about 8.3 generations. When the yeast was treated with nicotinamide riboside, the average life span nearly doubled, to 16.1 generations.

And in a model commonly used to study life span modifications, researchers discovered that the roundworm C. elegans could be made to survive, on average, 16% longer when supplemented with nicotinamide riboside; this life span extension was demonstrated to result from a roughly 50% increase in mitochondrial oxygen consumption, a measure of mitochondrial efficiency.

When pursuing additional lab studies, scientists found that supplementing mice with nicotinamide riboside reduced many dangerous factors of aging. For one particular study, the mice were fed a high-fat diet with either no supplementation (control), or nicotinamide riboside for 12 or 16 weeks. The supplemented mice showed healthy weight loss, increased energy, and improved insulin sensitivity, all of the factors that indicate optimal vitality. The scientists also demonstrated that nicotinamide riboside

A Novel Form of Vitamin B3 Switches “Off” Aging Genes

- Normal aging is in part the result of declining levels of NAD+, an essential compound found in every cell. Boosting levels can promote youthful vitality and even extend life span.
- The most effective way to boost NAD+ levels is through nicotinamide riboside, a newly discovered form of vitamin B3.
- Studies have found that nicotinamide riboside switches “off” the genes of aging, increases endurance, improves cognitive function, activates the key anti-aging sirtuins SIRT1 and SIRT3, enhances cellular energy, and extends life span.
supplementation increased energy metabolism while protecting the animals against the metabolic abnormalities induced by a high-fat diet.\(^{11}\)

Remarkably, these beneficial results were attained without any differences in food intake or total physical activity between supplemented and control mice.\(^{11}\) The supplemented animals lost weight, performed better at exercise, and managed their blood glucose better purely as a result of nicotinamide riboside-induced increases in calorie-burning (measured by increased oxygen consumption rates).

Detailed analysis of the mice in this study revealed that supplementation with nicotinamide riboside had produced a marked increase in essential NAD\(^+\) levels, resulting in the activation of the critical life span-extending enzymes SIRT1 and SIRT3.\(^{11}\) Supplementation with nicotinamide riboside also improved the numbers and function of mitochondria.

**Nicotinamide Riboside Protects Brain Cells**

As cases of dementia and Alzheimer’s reach epidemic proportions in the aging population, pharmaceutical companies are aggressively researching neuroprotective compounds.\(^{35,46}\) Nicotinamide riboside, with its ability to directly increase NAD\(^+\), is providing promising brain benefits.

A recent lab study demonstrated the ability of nicotinamide riboside to protect brain cells in advanced age.\(^{15}\) For the study, mice that were engineered to develop Alzheimer’s disease were treated with nicotinamide riboside beginning at middle age (5 to 6 months) and lasting into old age (10 to 11 months). At the end of the study, the supplemented animals had significant improvements in their cognitive function.\(^{15}\) The mechanisms by which these effects were achieved were found to include significant increases in brain levels of NAD\(^+\) (the result of supplementation with nicotinamide riboside) and consequently activated enzymes involved in cellular energy production and energy release from glucose.\(^{15}\)

In a similar study of neuroprotection, nicotinamide riboside was shown to delay the degeneration of axons, the “communications cables” of nerve cells that carry impulses over long distances.\(^{47,48}\) When these communication cables deteriorate, tingling, weakness, numbness, and loss of motor function can occur as a result.\(^{49,51}\)

Other studies in mammalian cells in culture demonstrate that nicotinamide riboside treatment increases NAD\(^+\) concentrations inside of cells by up to 2.7-fold,\(^{52}\) and that administering nicotinamide riboside can improve NAD\(^+\)-related deficiencies in animal and yeast cells.\(^{53}\)
Summary

Nicotinamide riboside is a unique form of vitamin B3 that has been found to provide an extraordinary range of impressive longevity benefits that promise to change how science approaches the reduction of aging.

By boosting levels of a powerful molecule called NAD+, nicotinamide riboside switches “off” many deleterious genes of aging, extends life span, increases endurance, improves cognitive function, activates sirtuins, and enhances cellular energy.

Directly boosting NAD+ with nicotinamide riboside presents a new and effective strategy for preventing the natural decline in cellular energy as we age by promoting youthful vitality.

If you have any questions on the scientific content of this article, please call a Life Extension® Health Advisor at 1-866-864-3027.

References


Tart cherries are packed with unique compounds that have been shown to block the COX-1 and COX-2 inflammatory enzymes. The benefits of tart cherry include rapid muscle recovery after exercise and fast relief from the minor aches, discomfort, and stiffness that can follow everyday muscle exertion.

Clinically Validated

In human studies, researchers have scientifically confirmed the muscle-supporting benefits of tart cherries. For example, a randomized controlled trial found that consuming tart cherry juice twice daily produced a substantial decrease in muscle symptoms related to exercise. In the same study, the exercise-induced loss of strength over the four days following a workout was reduced from 22% to only 4%.

Anthocyanins

Anthocyanins are powerful flavonoids that provide the dark pigmentation in blueberries, raspberries, and bilberries. What has drawn the attention of scientists is that tart cherries contain a higher content of anthocyanins than other fruits.

Anthocyanins have been extensively studied for their numerous advantages that include heart, cellular, and cognitive health.

Life Extension now offers 100% natural Tart Cherry Extract, a supplement that opens the door to the remarkable benefits of continued physical activity—at any age! This formulation provides all the muscle-supporting benefits of tart cherries and mimics the anthocyanin dose used in successful clinical trials by providing a standardized 40 mg dose of anthocyanins in each capsule.

The serving size of one vegetarian capsule of Tart Cherry Extract with Standardized CherryPURE® contains:

- CherryPURE® Tart cherry (Prunus cerasus) extract (skin) 615.5 mg [std to 6.5% anthocyanins (40 mg)]

A bottle of 60 vegetarian capsules of Tart Cherry Extract with Standardized CherryPURE® retails for $22. If a member buys four bottles during Super Sale, the price is reduced to $13.50 per bottle.

CherryPURE® is a registered trademark of Shoreline Fruit, LLC.

References

To order Tart Cherry Extract with Standardized CherryPURE®, call 1-800-544-4440 or visit www.LifeExtension.com

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.
Advanced Defense Against Cellular Aging

NAD+ Cell Regenerator

If you are experiencing fatigue and lack of motivation, it may be due to the age-related decline in NAD+ levels and subsequent impairment of healthy cellular metabolism.2

NAD+ (nicotinamide adenine dinucleotide) promotes systemic youthful functions and is found in every cell in the body.3 In addition, NAD+ plays an essential role in regulating genes4,5 that control aging.6

How To Boost NAD+ Levels Within Your Cells

Newly patented nicotinamide riboside increases cellular levels of NAD+ in the body.7,8

For the first time, aging humans have an effective and affordable method to boost the critical NAD+ enzyme for refreshed vitality.

Nicotinamide riboside represents an innovative advance to combat aging that functions via unique mechanisms not found in typical dietary supplements. It has emerged as a front-line weapon in Life Extension’s ongoing war against premature aging.

The name of this new nicotinamide riboside formulation is NAD+ Cell Regenerator™.

Multiple Benefits Of Increasing NAD+ Cellular Levels

Nicotinamide riboside has been documented to help replenish cellular NAD+ and in the process:

- Promote sirtuin (SIRT1 and SIRT3) gene activation,6
- Enhance growth and efficiency of mitochondria—supporting energy levels and physical performance,6
- Favorably modulate metabolism,6
- Contribute to neuronal health—supporting cognitive function during aging,9,10
- Promote insulin activity—supporting healthy blood sugar in those within the normal range.6

Life Extension® NAD+ Cell Regenerator™ contains the patented ingredient NIAGEN®, the first commercially available form of nicotinamide riboside.

The suggested daily dose of one NAD+ Cell Regenerator™ capsule provides:

NIAGEN® Nicotinamide Riboside 100 mg

Advanced NAD+ Technology At A Low Price

A bottle of 30 vegetarian capsules of NAD+ Cell Regenerator™ retails for $34. If a Life Extension member buys four bottles during Super Sale, the price is reduced to $17.55 per bottle. The suggested dose is just one small capsule daily.

NIAGEN® is a trademark of ChromaDex, Inc.

To order NAD+ Cell Regenerator™, call 1-800-544-4440 or visit www.LifeExtension.com

References
Over 6,000 studies have been published on resveratrol, a compound shown to favorably alter genes that help slow the aging process. In fact, resveratrol triggers some of the same beneficial youthful gene expression activated by calorie restriction.¹

The all-new Optimized Resveratrol with NAD+ Cell Regenerator now contains NIAGEN® nicotinamide riboside, a novel nutrient shown to support mitochondrial health and promote longevity pathways. This new formula provides 100 mg of NIAGEN® nicotinamide riboside—an amount equivalent to almost 667 cups of milk!²

The updated Optimized Resveratrol with NAD+ Cell Regenerator also contains specific compounds in berries, such as pterostilbene and fisetin, which researchers say work in synergy with resveratrol to “turn on” the body’s own longevity genes.

Advanced Defense Against Cellular Aging

The all-new...

OPTIMIZED RESVERATROL

with NAD+ Cell Regenerator

Just one capsule of Optimized Resveratrol with NAD+ Cell Regenerator supplies:

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Amount</th>
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<tbody>
<tr>
<td>Trans-Resveratrol</td>
<td>250 mg</td>
</tr>
<tr>
<td>NIAGEN® Nicotinamide Riboside</td>
<td>100 mg</td>
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<tr>
<td>Grape-Berry Actives</td>
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<td>Quercetin</td>
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<td>Trans-Pterostilbene</td>
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<tr>
<td>Fisetin</td>
<td>10 mg</td>
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A bottle of 30 Optimized Resveratrol with NAD+ Cell Regenerator vegetarian capsules retails for $42 (Item # 01930). If a member buys four bottles during Super Sale, the price is reduced to $24.30 per bottle. The suggested dose is one capsule daily of this “optimized” resveratrol formula.

Nicotinamide Riboside NIAGEN® is a registered trademark of ChromaDex, Inc. Patents see: www.ChromaDexPatents.com.

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References

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Every December, thousands of physicians attend what is by far the largest anti-aging conference in the world: the A4M (American Academy of Anti-Aging Medicine) conference in Las Vegas, Nevada. I have attended many of these conferences, most recently in 2012 and 2013. I will report mainly on the 2013 conference, but will include a few relevant presentations made at the 2012 A4M conference.
Endothelial dysfunction contributes to high blood pressure and atherosclerosis and precedes atherosclerosis years before the disease manifests. Endothelial dysfunction tends to occur in men at an earlier age than it occurs in women.

Pomegranate protects cardiovascular health by augmenting nitric oxide, which supports the functioning of endothelial cells that line the arterial walls. Nitric oxide signals vascular smooth muscle to relax, thereby increasing blood flow through arteries and veins.

Scientists have known for some time that oxidized LDL (low-density lipoprotein) can reduce the expression of nitric oxide synthase, the enzyme that produces nitric oxide from an amino acid called arginine. Recently, they discovered that pomegranate juice enhances the bioactivity of nitric oxide synthase in endothelial cells. Furthermore, pomegranate’s antioxidant properties protect nitric oxide from oxidative destruction, thus augmenting its biological actions.

An Italian study examined the role of pomegranate juice in nitric oxide synthase activity in artery sections that had already developed atherosclerosis. In these segments, blood forcing its way around atherosclerotic plaque buildup exerts significant stress on arterial walls. This stress reduces nitric oxide synthase expression and sets the stage for the formation of yet more plaque.

The researchers selected mice with a genetic predisposition to developing atherosclerosis. They put the mice in one of the groups on a high-fat diet, let arterial disease develop for six months, and then added pomegranate juice to the experimental group’s drinking water for 24 weeks. The placebo group was given plain drinking water.

Pomegranate not only increased the expression of nitric oxide synthase in both healthy and atherosclerotic blood vessels, but increased it the most in blood vessels with the most plaque buildup. The list below shows the increase in nitric oxide synthase expression that occurred in response to pomegranate:

- Healthy blood vessel areas
  - 3.3% increase in nitric oxide synthase
- Low-prone atherosclerotic areas
  - 26.1% increase in nitric oxide synthase
- High-prone atherosclerotic areas
  - 46.7% increase in nitric oxide synthase

Pomegranate’s ability to increase nitric oxide synthase resulted in a significant reduction in atherosclerotic lesions.
High Blood Pressure: Diagnosis And Treatment

Mark C. Houston, MD, (Associate Clinical Professor of Medicine, Vanderbilt University School of Medicine, and Director of the Hypertension Institute, Saint Thomas Hospital and Health Services) said that high blood pressure is due to three stressors to the endothelial cells that line blood vessels: inflammation, oxidative stress, and immune dysfunction.

Dr. Houston said that endothelial dysfunction precedes high blood pressure by decades. Once high blood pressure develops, blood vessel disease gets worse, creating a vicious cycle. To the extent that inflammation is part of this vicious cycle, high blood pressure is an inflammatory disease.

Dr. Houston described different methods of measuring blood pressure. Manual measurement of blood pressure in a medical office is the worst method. The “white-coat response” (anxiety in reaction to medical professionals) can result in an elevated blood pressure reading leading to unnecessary drug therapy. This effect can be eliminated by the use of an automated device. Even better is a blood pressure monitoring device that can be worn over a 24-hour period. Patients whose blood pressure does not decrease while sleeping are more likely to have a stroke. Unfortunately, wearing a blood pressure monitoring device at night can often disturb sleep, undermining the accuracy of the reading.

Dr. Houston has had great success in getting his patients off blood pressure drugs with his program of diet, exercise, weight reduction, and supplements. After six months of his treatment protocol, 62% of his high blood pressure patients were able to stop taking drugs. According to Dr. Houston, the average American is consuming about 10 times the minimum requirement for sodium, and is consuming two times as much sodium as potassium. Consuming five times more potassium than sodium is recommended. For blood pressure reduction, Dr. Houston also recommends omega-3 fatty acids (especially DHA), a monounsaturated fat (such as olive oil), vitamin C, vitamin D, lycopene, pycnogenol, coenzyme Q10, and 500 to 1,000 mg per day of magnesium.

Testosterone Replacement Does Not Cause Prostate Cancer

Abraham Morgentaler, MD, (Associate Clinical Professor of Urology, Harvard Medical School) has helped revolutionize testosterone replacement for older men. Prior to the 1990s, it was commonly believed that administering testosterone increased the risk of prostate cancer. Dr. Morgentaler began questioning this belief when he found evidence of prostate cancer in biopsies in men having low testosterone. In 1996, he published a paper in the Journal of the American Medical Association, which documented prostate cancer in 11 (14%) of 77 men with low testosterone. This result suggested to him that low testosterone is a risk factor rather than a protective factor for prostate cancer.

A decade later he was able to report that clinical trials with testosterone replacement therapy showed no increase in risk of prostate cancer. High serum testosterone is not associated with a risk of developing prostate cancer. Testosterone replacement therapy does not even increase cancer in men with a high risk of prostate cancer.

Dr. Morgentaler hypothesized that testosterone can facilitate prostate cancer if given to men with extremely low levels of testosterone. But this effect quickly reaches saturation due to the limited number of testosterone receptors. His analogy is that once a plant is receiving enough water, additional water does not make the plant grow more.

Whereas normal blood testosterone is typically well above 450 ng/dL, saturation is estimated to occur at 230 ng/dL total serum testosterone. For this reason, a man with serum testosterone of 250 or 300 ng/dL would be testosterone deficient, but would be above the level at which testosterone therapy could increase prostate cancer risk. An estimated 20% of men have low testosterone by age 50, while half of men have low testosterone by age 80. Low testosterone levels are associated with decreased muscle mass, low bone density, central obesity, insulin resistance, low energy, decreased cardiovascular health, low libido, and irritability. Also, it is associated with increased mortality in the elderly population.
In 2004, Dr. Morgentaler was writing a review of evidence for the safety of testosterone replacement therapy when it occurred to him to search for the basis of earlier beliefs that testosterone therapy would increase prostate cancer risk. He discovered the source to be a single study based on a single unrepresentative patient in 1941 by Nobel Laureate Charles Brenton Huggins.

Dr. Morgentaler gave presentations at both the 2012 and 2013 A4M. About 85% of his 2013 presentation was identical to his 2012 presentation. Most of the new material in his 2013 presentation was a response to a recent article claiming that testosterone therapy increases cardiovascular disease risk. Dr. Morgentaler cited evidence to the contrary, calling the study flawed. His opinion was shared by other scientists.

Benefits And Hazards Of Playing Football

Joseph Maroon, MD, (Professor of Neurological Surgery, University of Pennsylvania School of Medicine) addressed the question, “Should you allow your child to play football?” Dr. Maroon cited the risks, but also extolled the benefits, which are not as easily scientifically documented.

Between 1980 and 2006, out of millions of players, there were 1,866 documented deaths or survived cardiac arrests in American competitive athletics; 56% of these deaths were due to cardiovascular disease, compared to 22% caused by trauma. Cardiovascular deaths in athletes under age 40 are usually due to inherited conditions. Retired professional football players, however, suffer more cardiovascular disease than the general population their same age. The injury rate among American high school athletes in the 2005-2006 school year was highest in football (4.36 per 1,000 athletes), followed by wrestling (2.5 per 1,000 for boys). Dr. Maroon stated that injuries from riding bicycles exceeded those from football and asked, “Should you allow your child to ride a bicycle?”

Dr. Maroon has devoted a great deal of attention to the subject of concussion. Long-term consequences of concussion include brain pathology from tau protein that is similar to what is seen in Alzheimer’s disease. Dr. Maroon recommended omega-3 fatty acids to reduce possible effects of concussion. He also referred to the Lystedt Law, passed in Washington State in 2009 (and subsequently passed in most other states), requiring that athletes under the age of 18 who have experienced concussion during a practice or game be prohibited from further participation until cleared by a medical professional. The majority of coaches were already avoiding returning an athlete to play too soon after a suspected concussion.

Dr. Maroon’s concluding remarks included a personal testimony regarding the benefits to health and character resulting from his lifelong participation in athletics. He contrasted the alarming growth of childhood obesity with the health benefits, social skills, and leadership skills that arise from athletic competition. He quoted General Douglas MacArthur, who wrote, “Upon the fields of friendly strife are sown the seeds that upon other fields, on other days, will bear the fruits of victory.”

Daniel Amen, MD, (Psychiatrist and Medical Director of Amen Clinics, Inc.) spoke at the 2012 Las Vegas A4M conference with a message that conflicted with Dr. Maroon’s. Dr. Amen said that, “You should only allow your kids to play tackle football if you don’t like them.” He added that brain damage can occur even without concussion, referring to disrupted white matter found in the brains of soccer players rather than swimmers.

Dr. Amen specializes in SPECT (Single Photon Emission Computed Tomography), which uses gamma rays to image the brain. He has established that SPECT is superior to other brain imaging techniques, namely CT (Computed Tomography) or MRI (Magnetic Resonance Imaging), for the detection of mild traumatic brain injury. SPECT accuracy in diagnosis of Alzheimer’s disease may be as high as 88%. Dr. Amen is critical of other psychiatrists for not examining the organ which they are studying—the brain. Dr. Amen believes he has established that SPECT can reveal undetected brain traumas, brain toxicities, and other maladies leading to psychiatric symptoms. Dr. Amen has determined that overweight and obese persons have smaller brain volume...
metabolic syndrome, and alcohol-induced liver damage. MitoQ became the first molecule designed to reduce mitochondrial oxidative damage to enter phase II clinical trials. One trial, intended to reduce Parkinson's disease, failed to show any benefit, probably because the neuron damage in the patients was already too great for the chemical to have an effect. But the other trial, on hepatitis C, demonstrated that MitoQ could decrease liver inflammation in patients suffering from the disease. Future clinical trials are planned.

**Detoxification Strategies**

John Cline, MD, (Medical Director, Cline Medical Center, Nanaimo, BC, Canada) described his methods of detoxification. Dr. Cline is more representative of “alternative medicine” than the other presenters. Chelation therapy (removal of toxic metals from the blood) is part of his practice. Dr. Cline also recommended infrared saunas for elimination of toxic metals from the body. Arsenic, cadmium, lead, and mercury are toxic metals that have no known beneficial effect in humans, but which can be removed from the body through sweating.

The human body normally detoxifies chemicals through two-step metabolic processing in the kidney, described as phase I and phase II biotransformation. First, phase I causes a chemical alteration of the toxin through oxidation, reduction, or hydrolysis. Dr. Amen has also shown reduced blood flow in the brains of retired professional football players, which he says is consistent with a pattern of chronic brain trauma. Dr. Amen said that helmets prevent skull fracture, but not brain injury. The skull is hard, whereas the brain is soft and when there is trauma to the head, the soft brain slams up against bony ridges. In his experience, many psychiatric problems can be traced to undetected head traumas. He reported improved blood flow in retired professional football players who he treated with fish oil, multiple vitamins, ginkgo, alpha lipoic acid, and N-acetyl-cysteine.

**MitoQ For Mitochondrial Dysfunction**

Michael Murphy, PhD, (Group Leader, Medical Research Council Mitochondrial Biology Unit, Cambridge, England) said that many aging-related diseases are the result of increasingly dysfunctional mitochondria (the organelles that provide energy to cells). Because getting drugs or nutraceuticals into mitochondria can be difficult, Dr. Murphy (as a mitochondrial biochemist) designed a new antioxidant molecule tailored for entering mitochondria. He called his new molecule MitoQ. Modeling a variety of diseases in mice and rats, Dr. Murphy demonstrated the potential benefit of MitoQ against cardiac ischemia-reperfusion, sepsis, diabetic nephropathy, multiple sclerosis, inflammatory bowel disease, and metabolic syndrome, and alcohol-induced liver damage. MitoQ became the first molecule designed to reduce mitochondrial oxidative damage to enter phase II clinical trials. One trial, intended to reduce Parkinson's disease, failed to show any benefit, probably because the neuron damage in the patients was already too great for the chemical to have an effect. But the other trial, on hepatitis C, demonstrated that MitoQ could decrease liver inflammation in patients suffering from the disease. Future clinical trials are planned.
Dr. Collins achieved fame by showing that defects in telomerase (the enzyme that lengthens telomeres) are linked with a genetic disease called dyskeratosis congenita, which is associated with bone marrow failure. Later it was shown that short telomeres could be used as a means of identifying patients who have the genetic defect leading to bone marrow failure. Dr. Collins said there is evidence that telomere length could be used as a diagnostic tool to identify women who have genetic defects that make them at high risk for developing breast cancer. She noted that short telomeres can be indicative of an unhealthy lifestyle, including smoking, obesity, consumption of processed meats, and a low intake of vitamin D or omega-3 fatty acids. Dr. Collins believes that measuring telomere length could be a useful tool in the coming age of molecular medicine based on the genomic, metabolic, and antibody profile of individual patients. But she said that too often, the average telomere length is used as a diagnostic tool rather than the lengths of the shortest telomeres in cells. Determining the length of the shortest telomeres is important because it is the shortest telomeres that cause cells to become dysfunctional. At the conference, Dr. Collins was representing the company Life Length (www.lifelength.com), which specializes in measuring shortest telomeres. Dr. Collins was occupying the Life Length booth in the A4M exhibit hall.

Mark Rosenberg, MD, (Physician, Institute for Healthy Aging, Boca Raton, Florida) noted that although telomerase is present in the great majority of cancer cells, short telomeres can lead to cancer by causing chromosome abnormalities. A study of average telomere length of white blood cells showed that the group of people with the lowest third of telomere lengths were three times more likely to get cancer and two times as likely to die of cancer over a 10-year period as people in the highest third of telomere lengths. Similarly, persons whose white blood cell telomeres are short have a higher risk of developing coronary heart disease, and are eight times more likely to die of infectious disease. Mice that were bred to be cancer resistant had their life spans increased by the telomerase enzyme (which lengthened their telomeres).

There is a concern that lengthening telomeres by increasing telomerase activity can facilitate cancer. But mice whose telomerase activity was increased by gene therapy at 1-year or 2-years of age had a 24 or 13% (respectively) increase in median life span without increased cancer risk. In adult mice, at least, increasing telomerase activity had health benefits without increased cancer risk, which could be a promising sign for humans. The health benefits for the mice...
included increased insulin sensitivity and improved neuromuscular coordination. Dr. Rosenberg gave evidence of increased telomere length in people who take supplements. Average white blood cell telomere length was 5% longer for women who took multivitamin supplements, and higher dietary intakes of vitamins C and E were also associated with longer telomeres. Longer telomeres were associated with higher plasma levels of folic acid, vitamin D, and omega-3 fatty acids, as well as higher dietary intake of magnesium and curcumin.

William Andrews, PhD, (Founder and President of Sierra Sciences) believes that human health and longevity without risk of cancer can be achieved by activating telomerase, the enzyme that lengthens telomeres. He noted that telomerase is active in lobsters, which continue to grow throughout their whole lives, rather than ceasing to grow at an age of maturity. But lobsters do not get cancer, even in polluted waters that increase cancer in fish and molluscs. Dr. Andrews created his company Sierra Sciences for the purpose of discovering chemicals that could increase the activity of telomerase enzyme. Telomerase preferentially lengthens the shortest telomeres in human cells. The highest potency substance Dr. Andrews has found so far is a chemical that stimulates telomerase activity to 16% of the amount that would be required to make cells immortal. He believes that with $30 million he could achieve 100%.

If you have any questions on the scientific content of this article, please call a Life Extension* Health Advisor at 1-866-864-3027.

References


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GET SERIOUS
A Neurosurgeon’s Guide
To Optimal Health And Fitness

With Brett A. Osborn, DO, FAANS, CSCS

Brett A. Osborn, DO, FAANS, CSCS, is a neurological surgeon with a secondary certification in anti-aging and regenerative medicine—and a Life Extension® member. He specializes in scientifically based nutrition and exercise and is a walking billboard for his recommended regimen. His book, Get Serious, A Neurosurgeon’s Guide to Optimal Health and Fitness, teaches that we need to take responsibility for our own health and longevity. In this exclusive interview, Dr. Osborn talks about some of the key recommendations in his book.

LE: Dr. Osborn, to what extent do our genes predetermine our health and longevity?

BAO: The truth is most ailments of modern-day society are preventable. Yes, most strokes, dementia, heart attacks, diabetes, spine disorders, and even most cancers, are preventable... You are ultimately in control. So stop blaming your genes! Keep in mind that the majority of diseases—barring those of a congenital nature—are environmental in origin.
LE: Even cancer?

BAO: Yes, this even includes cancer! It was previously thought that if one developed cancer, he or she “had bad genes.” Cancer was “genetic.” Cancer is largely an environmental disease, period. As many as 90 to 95% of all types of cancers have their roots in the environment and lifestyle. As noted in a study published in Pharmacology Research, a respected, mainstream medical journal, “The evidence indicates that of all cancer-related deaths, almost 25 to 30% are due to tobacco, as many as 30 to 35% are linked to diet, about 15 to 20% are due to infections, and the remaining percentage are due to other factors like radiation, stress, physical activity, environmental pollutants, etc.” You and you alone have a choice, a choice to be healthy or sick. And this choice is independent of the hand your parents dealt you.

LE: Angelina Jolie recently had a prophylactic double mastectomy based upon the results of genetic testing.

BAO: Well, here’s the deal. There are specific genes, which if mutated, are associated with the development of certain cancers—BRCA1 and BRCA2 in the context of breast cancer. If high-risk individuals harboring these mutations were identified, they potentially could intervene early, thereby preventing disease. Keep in mind, however, that the incidence of the BRCA mutation in the general population is low. According to the American Heart Association, heart disease claims nearly 500,000 women yearly. This is nearly 12 times more than reported breast-cancer related deaths in 2009. Accordingly, educating the public about this preventable disease should be more the focus of our attention than radical celebrity-endorsed procedures that will benefit relatively few, specifically those with the gene.

LE: In your book, you suggest we should lump cancer and other lethal diseases together and search for a common cause, correct?

BAO: The answer is a resounding YES! In recent years, inflammation has come to the forefront as a major player in the genesis of atherosclerotic heart disease, cerebrovascular disease, diabetes, and cancer. From my standpoint, all diseases have an inflammatory component, all of them. And this is where we should focus our efforts primarily, from a preventive standpoint. Hunting down genetic mutations in existing tumors is too late. Instead, we should be preventing the genetic mutations and protecting the genome by limiting free-radical production and reducing oxidative stress. This will ultimately reduce the incidence of all diseases, not just cancer, as most have similar origins.

LE: But inflammation is protective of the body.

BAO: Restated, acute inflammation is protective of the body. It is integral to our immune response, wound healing and repair of exercise-induced muscle damage... Chronic inflammation on the other hand serves absolutely no benefit. Unfortunately, in many of us, this flame burns unchecked and disease accumulates. Blame no one except yourself and certainly not your genes. You are “insulting” your genes by presenting them with bad stimuli such as poor nutrition, tobacco smoke, and a lack of exercise. Chronic exposure to excess free radicals (oxidation) and inflammation cause age-related disease. Oxidation and inflammation are like two peas in a pod. Where there is one, there’s the other.

LE: How can we determine our inflammation levels?

BAO: Have your CRP checked. CRP, or C-reactive protein, is a protein secreted by the liver in response to a variety of stimuli, namely those associated with inflammation. For example, CRP levels increase with inflammation from infections, cardiovascular disease, and cancer. Elevated CRP levels are also associated with a higher risk of heart disease and stroke. However, CRP levels can be lowered by lifestyle changes such as smoking cessation, weight loss, increased physical activity, and a healthy diet.
that activate the inflammatory cascade. Interestingly, one of the factors that causes an elevation in CRP levels is secreted by adipocytes or fat cells. It should not come as a surprise, therefore, to learn that patients with metabolic syndrome have elevated CRP levels. In fact, CRP is an independent risk factor for coronary heart disease, hypertension, type II diabetes, and atherogenic dyslipidemia. Do not procrastinate and allow bodily inflammation to run rampant one day longer. Stop inflammation in its tracks with proper nutrition, exercise, supplements, and, if need be, pharmaceuticals. Drive your [high-sensitivity CRP test results] down [toward] zero. This is an indication that you are doing something right.

**LE:** Your book stresses that both saturated and unsaturated fats are essential to health. But aren’t saturated fats bad for us?

**BAO:** [They’re] not as bad as was once thought. Ironically, their cautious consumption may confer protection against a variety of diseases. On the other hand, unsaturated fats are not all “good.” Omega-3 fatty acids isolated from cold water fish, yes; omega-6 fatty acids in the context of the American diet, no. Allow me to explain. Saturated fat in the presence of high glycemic index carbohydrates—or reduced levels of “good” polyunsaturated fats—elevates LDL or “bad” cholesterol levels. On its own, it doesn’t.

**LE:** So it’s beneficial to consume saturated fat?

**BAO:** Right, but only under favorable conditions. Low insulin levels are mandatory, as is high dietary omega-3 fatty acid intake. Unfortunately, the typical American diet fosters high insulin levels, lacks adequate omega-3 fatty acids, and is replete with omega-6 fatty acids, which in excess are inflammatory in nature. This milieu is atherogenic, or artery clogging. To prevent heart disease, the number one killer of Americans, and to potentially reduce the incidence of certain cancers among many other diseases, one must alter the omega-6:omega-3 ratio. I’m not a fish eater, yet I take high-dose omega-3 capsules. For me, it’s not an apple a day, but an oil change a day that keeps the doctor away.

**LE:** So what is cholesterol and how risky are high levels of it?

**BAO:** Cholesterol is vital to our existence, as are fats. This waxy substance is the precursor of many hormones including cortisol, testosterone, progesterone, and estrogen. In fact, it is considered the “mother of all hormones.” Cholesterol is also a crucial component of cell membranes, including the myelin sheaths of neurons. Unfortunately, due to the aggressive scare tactic-based marketing schemes utilized by Big Pharma, most individuals with “high cholesterol” are prescribed statins as a preventive modality for coronary heart disease. Well guess what? The data don’t pan out. A 2010 meta-analysis of more than 65,000 patients concluded that the use of statins in a high-risk primary prevention setting was not associated with a statistically significant reduction in the risk of all-cause mortality. Instead, concern yourself with the subtypes of LDL [cholesterol] floating around in your blood and your triglyceride: HDL ratio—each of which can be optimized with dietary interventions and not by default with statins.

**LE:** Doesn’t consuming less saturated fat lower LDL cholesterol?

**BAO:** While there may be a reduction in LDL when saturated fat intake is reduced, there is subtype shift from LDL “A” to “B,” hence an increased coronary
In his book, Get Serious, A Neurosurgeon’s Guide to Optimal Health and Fitness, Dr. Brett Osborn recommends his program for building a healthy, fit, and strong body and mind. Among his recommendations are key supplements. We asked him for his favorites and to explain the rationale for each choice.

**Omega-3 fatty acids:** If you could choose one, this would be it! There are literally volumes of data demonstrating the beneficial effects of omega-3s’ stemming from their robust anti-inflammatory capacity.

**Resveratrol:** In addition to providing robust anti-inflammatory effects, resveratrol influences the expression of several gene products that influence metabolism.

**Green tea extract:** Green tea has anticancer effects, probably through its epigallocatechin gallate, or EGCG content.

**Vitamin D:** You may not realize it, but vitamin D₃ is actually a hormone, a vital bodily hormone acting directly on the genome.

**Curcumin:** Curcumin has powerful anti-inflammatory properties which thwarts the formation of amyloid plaque.

**B-Complex:** B-complex vitamins are important for what is termed “methylation,” a cellular process that occurs a billion times per second. Deficient or “hypo” methylation is associated with a variety of diseases such as cancer, coronary artery and cerebrovascular disease, and neural tube defects.

**Vitamin C:** This is integral to numerous biological processes such as tissue repair, the quenching of free radicals, and the formation, along with the maintenance, of skin, tendons, ligaments, and blood vessels.

**Vitamin E (mixed tocopherols and tocotrienols):** The benefits of vitamin E are numerous. For example, supplementation has been demonstrated to reduce atherosclerotic plaque burden and improve one’s lipid profile.

**Magnesium:** Okay, there is no arguing about this one: Magnesium stabilizes the heart muscle and prevents arrhythmias. It lowers blood pressure by relaxing blood vessels, plays a role in carbohydrate metabolism, and reduces one’s risk of osteoporosis by augmenting bone density.

**Probiotics:** This is the good bacteria that most of us lack in our gut. Just because the bowel in actuality is external to the body does not permit you to neglect it. Nurture it, instead, for optimal health.

**And more:** Choose a multivitamin that is just that, “multi,” [as in] multiple capsules or tablets per day. While water is not considered a supplement, it should be. Even mild dehydration can affect mental and physical performance. Gastrointestinal function may also be impaired, resulting in delayed transit times and constipation.

### LE: How can we determine our LDL cholesterol subtypes?

**BAO:** VAP—Vertical Auto Profile—testing is a cholesterol, lipid, and lipoprotein test. It measures all the components of a standard lipid profile but delves further, segmenting cholesterol into subclasses. Subtype A is “fluffy” and less apt to be integrated into atherosclerotic plaque, while subtype B is dense and atherogenic. A standard lipid profile does not differentiate the two. For this reason, it is completely erroneous to assume that elevations in LDL are wholly bad. Your LDL may be composed mainly of subtype A.

### LE: In Get Serious, you explain that many pharmaceuticals have been shown to boost health in ways for which they were not specifically intended—but they are simply not offered to patients. Why not?

**BAO:** Because they are “off-label,” and doctors are quite frankly, nervous of lawsuits. And that’s a crying shame. Why? Because your doctor may be taking them!

### LE: Can you give us an example?

**BAO:** Statin drugs can lower cholesterol levels, but what you may not know is how many doctors—like me—are taking these.
drugs, even those who don’t have cholesterol problems. Why? Statins are also potent anti-inflammatory agents.

LE: You wrote that you also take the diabetes drug metformin.

BAO: Remember resveratrol? Well guess what: Metformin acts on similar enzymatic pathways, increasing insulin sensitivity, and by virtue, reducing the insulin signal. Reducing the insulin signal secondarily reduces inflammation in animal models. This likely occurs in humans as well, given the antitumoral effects metformin has on a variety of cancers. This effect, too, is the result of reduced growth factor expression in response to metformin. It acts at the level of the gene! And its actions are not limited to the insulin-signaling pathway; they are wide reaching, affecting and modulating many bodily processes. An analog of metformin will one day be launched as an “anti-aging” drug.

LE: Should everyone consider taking metformin now to inhibit aging—or wait for longevity studies?

BAO: [Metformin] mimics the effect of caloric restriction (CR). This significantly extends life in animal models. By reducing the insulin signal and therefore the risk of cancer, diabetes, vascular disease, and obesity, it will likely have similar effects in humans. Are you going to wait and see if it extends life prior to discussing this option with your doctor? I’ve been on metformin for years. Not a single untoward effect. And no, it typically does not make one hypoglycemic. Should you choose to take metformin, you must supplement with additional B vitamins, particularly B12 and folate.

LE: Your book addresses ways to build a stronger body. Is there a secret to adding muscle?

BAO: The only way to develop strength and build muscle is to progressively overload a muscle group through proper exercise. What is the optimal way to lose body fat and improve your physique? Aerobics? No. Resistance training. Weight lifting.

LE: No elliptical machines or other equipment or special classes?

BAO: The pillars of the training regimen will always be the five basic compound movements: squat, bench press, deadlift, overhead press, and a chin/pull-up or rowing movement. Whatever your goals, if you want to be big and muscular, or if you want to be nicely toned and sculpted, these basic exercises will get the job done. No balls or bikes or bands needed.

LE: In the chapter Supplements 101, you recommend particular nutritional supplements. How do you choose what supplements are most essential?

BAO: I chose my supplements logically, based upon what we know to be the agents of the aging process and particularly, age-related disease. And they are the same: free radical damage, oxidative stress, and chronic inflammation.

LE: Thanks a lot, Dr. Osborn.

BAO: Thank you.
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Researchers have discovered that the ceramides naturally produced by young skin are identical to those present in **wheat**—and that these wheat-derived oils can be taken **orally**.

Life Extension\(^5\) has brought together these skin-nourishing oils in a concentrated **oral formula** called **Skin Restoring Phytoceramides with Lipowheat\(^6\)**.

**Skin Restoring Phytoceramides with Lipowheat\(^6\)** can reach the deepest layers of skin all over the body—**not just where creams are applied**—where it can offset the visible impact of the body’s gradual decline in ceramides. The hydrating action of **Lipowheat\(^6\) ceramides** has proved effective in clinical trials.

One bottle containing **30 350 mg** vegetarian liquid capsules of **Skin Restoring Phytoceramides with Lipowheat\(^6\)** retails for **$25**. If a member buys four bottles during **Super Sale**, the price is reduced to **$15.53**.

Contains wheat.

**References**

**Lipowheat\(^6\)** is a registered trademark of LAVIPHARM Group of Companies.
ULTIMATE PROSTATE PROTECTION

At Life Extension®, we continually update our formulas to reflect the latest research findings.

Ultra Natural Prostate formula provides the latest scientifically validated, standardized botanical extracts shown to promote healthy prostate function. No other prostate protection formula provides such a broad array of nutrients to support the multiple factors involved in promoting the aging prostate gland. Here are the ingredients in the Ultra Natural Prostate formula:

- **Standardized lignans** convert to enterolactone in the intestine, which is then absorbed into the bloodstream to provide support for prostate cells against excess estrogen levels.1-3
- **AprèsFlex®** supports normal inhibition of 5-lipoxygenase or 5-LOX, an enzyme that is associated with undesirable cell division changes.4,5
- **Stinging and Dwarf nettle root extracts** help support prostate cells against excess estrogen levels.6,7
- **Saw Palmetto CO2 extract** helps inhibit dihydrotestosterone (DHT) activity in the prostate, helps support normal urinary flow, and helps regulate inflammatory reactions in the prostate.8-11
- **Pygeum (Pygeum africanum)** extract helps suppress prostaglandin production in the prostate and supports healthy urination patterns.12,13
- **Pumpkin seed oil**, from select pumpkins, enhances the composition of free fatty acids and augments saw palmetto’s benefits.14-16
- **Beta-sitosterol** enhances the protective effects of other botanical extracts and helps improve quality of life.17-19
- **Graminex® Flower Pollen Extract™** has been shown to help relax the smooth muscles of the urethra and help regulate inflammatory reactions.20-22
- **Boron** has been shown to slow elevation of prostate-specific antigen (PSA).23-25
- **Lycopene** supports efficient cellular communication, helps maintain healthy DNA, regulates hormonal metabolism, and promotes healthy prostate size and structure.26-32
- **Phospholipids** enhance absorption of active compounds.

A bottle of 60 softgels of Ultra Natural Prostate retails for $38. If a member buys four bottles during Super Sale, the price is reduced to $23.63 per bottle. If a member buys 12 bottles during Super Sale, the price is $21.60.

Contains soybeans.

To order Ultra Natural Prostate, call 1-800-544-4400 or visit www.LifeExtension.com

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

References

AprèsFlex® is a registered trademark of Laila Nutraceuticals exclusively licensed to TP. Thomas L. Lai, LLC. U.S. Patent No. 8,031,496 and other patents pending. HMRlignan™ is a trademark used under sublicense from Linnea S.A. US Patents 6,557,324 and 6,688,964. Albion® is a registered trademark of Albion Laboratories, Inc.
Milk thistle extract is one of nature's most potent weapons to support liver health. Until recently, however, the technology hasn't been available to fully harness this plant's full benefits.\(^1\)

The problem has been that the star component of milk thistle, called silybin, does not dissolve well in water.\(^2,3\) This makes it difficult for your body to absorb all of it.\(^2,3,4\)

Scientists have developed a novel technology to overcome silybin's poor bioavailability. The solution is to mix silybin with a nutrient called phosphatidylcholine.

**Phosphatidylcholine** facilitates transport across the intestinal lining into the bloodstream, making it an ideal "carrier molecule" for silybin.\(^3\) Scientists believe that phosphatidylcholine molecularly bonds to silybin, ushering it through the membranes of cells in the intestinal tract.\(^4\)

This unique silybin-phosphatidylcholine complex is absorbed nearly 5 \textit{times better} than silymarin alone, and its concentration in the liver, its target organ, is \textit{10-fold greater} than silymarin alone.\(^5-8\)

The suggested twice daily dosage of one softgel provides:

- **Milk Thistle Phospholipid Proprietary Blend**
  - 760 mg
  - Milk Thistle Extract (seed)
    - [providing silymarin (480 mg), Silybin (180 mg), and Isosilybin A and Isosilybin B (48 mg)], Phospholipids

- **SILIPHOS® Phytosome Milk Thistle Extract** (seed)
  - 160 mg
  - [providing 47.52 mg silybin]

A bottle containing 60 softgels of the \textit{absorption-enhanced} Milk Thistle retails for $28. If a member buys four bottles during Super Sale, the cost is reduced to $16.88 per bottle.

This novel Milk Thistle extract with phosphatidylcholine contains standardized concentrations of silybin and isosilybin A and B not found in other milk thistle extracts! Compare the price of Milk Thistle to commercial silymarin supplements, and members will see that this formula is available at one of the lowest costs per milligram.

Contains soybeans.

SILIPHOS® is a registered trademark of Indena S.p.A., Italy.

**To order** European Milk Thistle with Advanced Phospholipid Delivery call 1-800-544-4440 or visit www.LifeExtension.com

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\(^1\) Pak J Pharm Sci. 2008 Jul;21(3):249-54.
\(^3\) Indian J Pharmacol. 2007;39(4):172-79.
\(^5\) Available at: http://www.altmedrev.com/publications/77/2/15.pdf.
Chia
Nature’s Perfect Food

Recent studies have revealed that chia (*Salvia hispanica*) is a remarkably well-rounded nutritional source, providing protein, magnesium, phosphorus, and essential fatty acids. It is also the richest vegan source of omega-3 and dietary fiber. Gluten-free and grain-free, chia also has six times the calcium of milk.¹

Chia—which is Mayan for “strength”—is a desert plant native to Central America with edible seeds that have a pleasing, nutty flavor. A relative of the mint family, these little black and white seeds were once a staple of the ancient Aztec diet.²

Now, a growing body of research points to chia’s power to help prevent diseases such as cardiovascular disorders,³,⁴ cancer,⁵ and diabetes.⁴ But above all, experts now recognize the remarkable weight-reducing capacity of chia seeds,⁶,⁷ which are often referred to as “a dieter’s dream.”
Lose Weight Without Starving

Hunger is a main enemy of weight loss. But tiny chia seeds quickly absorb a lot of liquid to create a gel8 that can keep you feeling full for hours. (This sticky gelatinous coating is how the seeds bonded to the popular terra cotta Chia Pets, which appear to grow hair overnight when watered.) When chia is exposed to water in the stomach, it increases in size and weight, and since the gel is made almost completely of water, it contains practically no calories. Since the gel coating continues to adhere tightly to each seed, it tricks the stomach into thinking it is full on just a fraction of the calories.9 Scientists have shown that chia decreases appetite for a full two hours after consumption and reduces the sugar spikes that occur after a meal.10 Because it absorbs 12 times its own weight, adding two tablespoons of chia to your diet reduces the energy density of food, while boosting fiber intake.9

Chia seeds are an excellent source of fiber, with 10 grams in two tablespoons—more than one-third of the daily recommended fiber intake.10 Both the chia gel and fiber content help food move through your digestive tract faster—removing toxins from the body more quickly to help prevent constipation, diarrhea, and diverticulosis.11

In a randomized clinical trial, volunteers with metabolic syndrome consumed a beverage containing chia. After two months, those who consumed the chia had a greater decrease in body weight than controls, as well as an increase in adiponectin—a hormone that plays a role in preventing obesity, metabolic syndrome, and type II diabetes.12-14 Adiponectin also exerts weight-loss effects on the body via the brain, similar to leptin, the satiety hormone.15 In this study, only the group consuming the chia beverage experienced decreases in serum triglycerides, in the inflammation marker C-reactive protein (CRP), and in the blood glucose response curve (AUC) after a glucose tolerance test.7

As an added bonus, Chia’s gelling action helps prolong hydration and retain electrolytes during exercise.

Inhibiting Diabetes

More than 29 million Americans now have diabetes and nearly 86 million have prediabetes, a condition of abnormally high blood sugar levels that falls just short of diagnosis for type II diabetes.16 Preclinical research suggests that chia supplementation can prevent the insulin resistance that leads to diabetes. In animals fed a sugar-rich diet, chia seeds were also shown to favorably modify blood lipid changes.4

If you eat high-starch or high-sugar foods, blood sugar is more likely to spike after meals, which can raise your risk of diabetes.17 Consuming chia with a meal can combat this by turning food into constant, steady blood-sugar energy, rather than a dangerous series of glucose ups and downs.

Chia gel creates a physical barrier between the carbohydrates you eat and the digestive enzymes that break them down into sugar. Chia’s high content of complete protein and its novel combination of soluble and insoluble fiber combine with the chia-gel barrier to slow down your body’s conversion of carbohydrates into blood sugar.8

Cardiovascular Support

Diabetes and its risk factors greatly increase the risk of cardiovascular disease. For those with type II diabetes, conventional medications and lifestyle changes alone often fail to significantly reduce the risk of heart disease.

Easy Egg And Butter Replacement

The tendency of chia to gel allows it to be used as an egg substitute in foods and baked goods, reducing dietary cholesterol and increasing nutrient content—as well as slashing calories. As a substitute for eggs, chia reduces calories and fat content, while not affecting taste, texture, color, or overall acceptability.26

To use as an egg replacement, simply mix one tablespoon of chia seeds with three tablespoons of water and let sit for 15 minutes.

Similarly, chia gel can replace half the butter in most recipes, since it bakes and and tastes the same or better. Simply divide the amount of butter called for in a recipe in half and make up the balance with chia.
Cutting-edge research has found that chia supplementation can provide enhanced cardiovascular protection specifically for diabetics. Vladimir Vuksan, PhD, of the Risk Factor Modification Center at the University of Toronto, Canada, has devoted significant resources to the study of chia’s beneficial effects on diabetics who are at risk for cardiovascular disease.3

In his most recent clinical trial, 20 adults with type II diabetes took supplements of either chia or wheat bran daily for three months. By the end of the study, the chia group saw significant improvement across a range of disease markers, including blood pressure and lipid profiles, as well as inflammatory and clotting factors. Systolic blood pressure in the chia group dropped by six points, while the wheat bran group’s blood pressure was unchanged. C-reactive protein and clotting factors were also markedly reduced in the chia group compared to the wheat bran group.3

Scientists found that, as a dietary fat source, chia could lower total cholesterol levels while increasing HDL cholesterol. They also found that when substituting chia seeds for other fat sources, such as corn oil, chia was able to prevent high triglyceride levels and reduce abdominal obesity. This was a result of chia’s high content of alpha linolenic acid (ALA), which is a precursor of omega-3 fatty acids.4

Chia’s rich content of fiber and phytochemicals, along with its unparalleled abundance of omega-3 fatty acids—the greatest omega-3 source of any plant—strongly promotes heart and cholesterol health. Along with its plentiful omega-6 fatty acids, the omega-3s in chia help build new cells and regulate body processes.2,3,10,18

Chia seeds contain a high proportion of the daily recommended intakes of calcium, magnesium and especially, manganese1,10—nutrients that may help prevent hypertension.19,20 These minerals are also important for healthy weight, energy metabolism, and DNA synthesis.

Osteoporosis Prevention

Many Americans are not getting nearly enough calcium, especially those who avoid dairy. This can cause osteoporosis, a disorder that decreases bone density and increases risk of fractures. Osteoporosis afflicts 54 million American adults,21 80% of whom are women. Millions more have osteopenia, a condition that is essentially pre-osteoporosis.21 By 2020, half of all Americans over age 50 will be at risk.21,22

Fortunately, a single ounce of chia seeds provides 18% of your daily calcium requirement—six times as much as an equal quantity of milk!1

Cancer Protection

Chia has shown additional promise in cancer prevention. In a pre-clinical study involving breast cancer models, researchers found that dietary chia inhibited both the overall growth and the spread of cancer.5

Chia’s Shelf Life

Chia contains properties that help combat premature aging of the skin and inflammation of various tissues.23,24 These same properties allow raw chia seeds to stay fresh and ready to eat for about four years, without deterioration in flavor, odor, or nutritional value—a quality not found in many seeds. Prepared chia gel will keep for up to two weeks, and can keep any food tasting fresh longer if the gel is mixed into it during preparation.

Ways To Use Chia

Chia seeds absorb the flavor of any liquid in which they are soaked, making for some interesting flavor combinations. For example, instead of water, try soaking chia in milk, vegetable juice, fruit juice, sauce, or nut milk. Add dry seeds to smoothies, granola, soups, sauces, or salads to lower calorie intake, boost nutritive value, and increase satiety.
Nutritional Content Of Chia

The abundance of fiber and essential fatty acids in chia packs a powerful nutritional wallop for minimal calories. A single ounce delivers 40% of your daily fiber requirement. Chia is the greatest source of omega-3 essential fatty acids of any plant food and provides high amounts of protein, calcium, phosphorus, and potassium.10

One ounce (or 28 grams) of dried chia seeds provides the following:10

<table>
<thead>
<tr>
<th>Percent Daily Value</th>
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<tbody>
<tr>
<td>Calories</td>
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<td>Calories from fat</td>
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<td>Calories from protein</td>
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<td>Saturated fat</td>
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<td>Cholesterol</td>
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<td>Zinc</td>
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<tr>
<td>Total Omega-3 fatty acids</td>
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<td>Total Omega-6 fatty acids</td>
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Summary

Growing research has shown the tiny Chia seeds to be a powerhouse that can help prevent diseases such as cardiovascular disorders, cancer, osteoporosis, and diabetes. But more importantly, it is recognized as “a dieter’s dream food” for its remarkable weight-loss capacity. Absorbing 12 times its own weight in liquids, studies have shown that chia decreases appetite for a full two hours after consumption, while reducing after-meal sugar spikes and providing 5 grams of fiber per tablespoon. •

If you have any questions on the scientific content of this article, please call a Life Extension Health Advisor at 1-866-864-3027.

References


If you have any questions on the scientific content of this article, please call a Life Extension Health Advisor at 1-866-864-3027.


Top Off Your TESTOSTERONE Naturally

Low Testosterone Levels May Lead to:
- Reduced Sex Drive
- Less Energy
- Cloudy Thinking
- Weight Gain
- Cardiovascular Issues

Maintaining healthy testosterone levels is one of the most important steps you can take to regain your health and improve your performance. With research showing that by the time a man is 60 years old, he may produce 60% less testosterone than he did in his 20s, the time is now to add Life Extension®’s Super MiraForte with Standardized Lignans to your supplement regimen.

The retail price for a bottle of 120 capsules of Super MiraForte with Standardized Lignans is $62. If a member buys four bottles during Super Sale, the price is reduced to $37.80 per bottle.

Each daily dose of Super MiraForte with Standardized Lignans contains the following testosterone supporting ingredients:

- 1,500 mg Chrysin
- 15 mg Bioperine®
- 850 mg Muira puama
- 282 mg Nettle root
- 15 mg Chelated elemental zinc
- 320 mg Maca
- 33.4 mg HMRlignan™

To order Super MiraForte with Standardized Lignans call 1-800-544-4440 or visit www.LifeExtension.com

Super MiraForte.

Caution: If you are taking any medication, use only under physician supervision. Men with existing prostate cancer may not be able to use this product. Elevations in free testosterone can unmask an occult (hidden) prostate cancer. Anyone with this concern should have a baseline PSA prior to using this product and a follow-up PSA test 60 days later. If a significant elevation of PSA is found, discontinue this product and advise physician. Do not take more than 15 mg per day of Bioperine®.

Bioperine® is a registered trademark of Sabinsa Corp. HMRlignan™ is a trademark used under sublicense from Linnea S.A.

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.
Profound loss of connections between nerve cells in the brain is one of the major hallmarks associated with neurodegeneration and memory impairment. Previous research has shown that magnesium is a critical factor in controlling synaptic density.¹

To combat this, an innovative form of magnesium called Neuro-Mag™ has been developed. The magnesium-L-threonate contained in Neuro-Mag™ has been shown to specifically target multiple areas of the aging brain. In fact, pre-clinical models show that the magnesium-L-threonate contained in Neuro-Mag™ boosted levels of magnesium in spinal fluid by 15% versus no increase from conventional magnesium.²

New Cognitive Benefits Revealed!

Although research into the role of magnesium in the brain dates back 70 years, scientists continue to uncover its comprehensive benefits for cognitive function.¹ Studies using magnesium-L-threonate show this unique form of magnesium maintains the quantity of synaptic connections between brain cells and inhibits the dysregulation of signaling pathways.¹

Capsules or Powder... Value Priced

The suggested daily dose of three Neuro-Mag™ Magnesium-L-Threonate Capsules provides 2,000 mg of Magnesium-L-Threonate. While supplying a modest 144 mg of elemental magnesium, its superior absorption into the bloodstream and nervous system make it a preferred choice for maturing individuals to supplement with.

This same brain-health supporting magnesium is also available in a natural lemon flavor called Neuro-Mag™ Magnesium-L-Threonate with Calcium and Vitamin D3 Powder. In addition to its fresh lemon flavor, the one-scoop per day serving supplies the same amount of magnesium as the capsules plus 500 mg of highly soluble calcium and 1,000 IU of vitamin D3.

A bottle containing 90 vegetarian capsules of Neuro-Mag™ Magnesium-L-Threonate or a jar containing 30 scoops of Neuro-Mag™ Magnesium-L-Threonate with Calcium and Vitamin D3 Powder retails for $30. If a member buys 4 units during Super Sale, the price is reduced to $24.30 per unit.

References
Blood testing provides the ultimate information regarding correctable risk factors that may predispose you to disorders such as cancer, diabetes, cardiovascular disease, and more. Information about general health and nutritional status can also be gained through standard blood analysis. Standing behind the belief that blood testing is an essential component of any program designed to attain optimal health and longevity, Life Extension® offers this innovative and convenient service at a very affordable price. Not only is comprehensive blood testing an important step in safeguarding your health, it is a simple process from virtually anywhere in the United States.

**Five Easy Steps:**
1. Call 1-800-208-3444 to discuss and place your order with one of our knowledgeable health advisors. (This order form can also be faxed to 1-866-728-1050 or mailed.)
2. After your order is placed, you will be mailed either a requisition form to take to your local LabCorp Patient Service Center or a Blood Draw Kit; whichever is applicable. (Please note: If a blood draw kit is used, an additional local draw fee may be incurred.)
3. Have your blood drawn.
4. Your blood test results will be sent directly to you by Life Extension.
5. Take the opportunity to discuss the results with one of our knowledgeable health advisors by calling 1-800-226-2370; or review the results with your personal physician.

It’s that simple! Don’t delay—call today!

**For Our Local Members:**
For those residing in the Ft. Lauderdale, Florida area, blood-draws are also performed at the Life Extension Nutrition Center from 9:00 am to 2:00 pm Monday through Saturday. Simply purchase the blood test and have it drawn with no wait! Our address is 5990 North Federal Highway, Ft. Lauderdale, FL, 33308-2633.
glucose over the past two weeks and is an
This test is used to aid in predicting risk for
Total and Free Testosterone, DHEA-S, Free T3, Free T4, Cortisol, C-Reactive Protein (high sensitivity), Vitamin B12, Folate, Insulin.

This test measures your average
associated with atherosclerosis. Lp-PLA2 is a
coronary heart disease, and ischemic stroke
cardiovascular risk factor that provides unique

This test measures their activity.
patrol the body looking for cells that are infected
inside your arteries.

This test is used to monitor SHBG levels which
deficiency as a cause of bone disease.

This test shows if you are taking the proper amount of DHEA. This test normally costs $100 or more at commercial laboratories.

This test measures serum concentrations of DHT.

For men and women. Determines the proper amount in the body.

Can predict those at risk of diabetes, obesity, heart and other diseases.

Used to determine ovarian failure, hirsutism, adrenal carcinoma, and Cushing’s syndrome.

Primarily for women. Determines the proper amount in the body.

This test shows if you are taking the proper amount of DHEA, Estradiol, Free and Total Testosterone, PSA

This test shows if you are taking the proper amount of DHEA, Estradiol, Free and Total Testosterone, Progesterone

Measures serum concentrations of DHT.

For men and women. Determines the proper amount in the body.

For non-member prices call 1-800-208-3444

For non-member prices call 1-800-208-3444
PRODUCTS

AMINO ACIDS
- Acetyl-L-Carnitine
- Acetyl-L-Carnitine-Arsinate
- Branched Chain Amino Acids
- D, L-Phenylalanine Capsules
- Glycine Capsules
- L-Arginine Capsules
- Arginine/L-Ornithine Capsules
- L-Carnitine Capsules
- L-Glutathione, L-Cysteine & C
- L-Glutamine Capsules
- L-Glutamine Powder
- L-Lysine Capsules
- L-Tyrosine Tablets
- Mega L-Glutathione Capsules
- N-Acetyl-L-Cysteine Capsules
- Optimized Carnitine with GlycoCarn®
- Pharma QABA®
- Super Carnosine Capsules
- Taurine Capsules

BONE & JOINT HEALTH
- ArthroMax® with Theaflavins and AprèsFlex®
- ArthroMax® Advanced with UC-II® and AprèsFlex®
- Bone-Up™
- Bone Restore
- Bone Restore w/Vitamin K2
- Bone Strength Formula w/KoAct™
- Dr. Strum’s Intensive Bone Formula
- Fast Acting Joint Formula
- Glucosamine Chondroitin Capsules

BRAIN HEALTH
- Acetyl-L-Carnitine
- Acetyl-L-Carnitine-Arsinate
- Brain Shield® Gastrodin
- Cognitex® with Brain Shield®
- Cognitex® with Pregnenolone & Brain Shield®
- Cognitex® Basics
- Cognizin® CDP Choline Capsules
- DMAE Bitartrate
- Ginkgo Biloba Certified Extract™
- Huperzine A
- Lecithin Granules
- Methylcobalamin Lozenges
- Migraine with Brain Shield®
- Neuro-Mag® Magnesium L-Threonate
- Optimized Ashwagandha Extract
- Phosphatidylserine Capsules
- Prevagen®
- Rhodiola Extract
- Super Ginkgo Extract
- Vinpocetine

DIGESTIVE
- Bilfo GI Balance
- Caromsorb® w/PicroProtect
- Digest RC™
- Esophageal Guardian
- Enhanced Super Digestive Enzymes
- Extraordinary Enzymes
- FlorAssist® Probiotic
- Gutsy Chewy Digestive Tablets
- Pancreatin
- Regimint
- Theracal Probiotics

DURK AND SANDY PRODUCTS
- Blast™
- Inner Power™

EYE CARE
- Bilberry Extract
- Brite Eyes III
- Eye Pressure Support with Mirtogenol®
- MacuGuard™ Ocular Support
- MacuGuard™ Ocular Support with Astaxanthin
- Solarshield Sunglasses
- Super Booster w/MacuGuard™ Ocular Support

FIBER
- AppleWise Polyphenol
- Fiber Food
- TruFiber®
- WellBetX PGX® plus Mulberry

FOOD
- Rich Rewards™ Black Bean Vegetable Soup
- Rich Rewards™ Spicy Cruciferous Vegetable Soup
- Rich Rewards™ Cruciferous Vegetable Soup
- Rich Rewards™ Lentil Soup
- Rich Rewards™ Mung Bean Soup with Turmeric
- Rich Rewards® Coffee (Available in mocha, vanilla and decaffeinated)
- Rich Rewards™ Protein Creamer
- Rich Rewards® Whole Bean Coffee

HAIR CARE
- Dr. Proctor’s Advanced Hair Formula
- Dr. Proctor’s Shampoo
- Super-Absorbable Tocotrienols

HEART HEALTH
- AppleWise Polyphenol
- Advanced Lipid Control
- Advance Olive Leaf Vascular Support w/Celery Seed Extract
- Aspirin (Enteric Coated)
- Cardio Peak™ w/Standardized Hawthorn and Arjuna Cho-Less™
- D-Ribose Tablets
- D-Ribose Powder
- Endothelial Defense™ with Full-Spectrum Pomegranate™
- Fibrinogen Resist
- Forskolin
- Homocysteine Resist
- Natural BP Management
- Peak ATP® with GlycoCarn®
- Policosanol
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- Pycnogenol® French Maritime Pine Bark Extract
- Red Yeast Rice
- Super Absorbable CoQ10™ w/d-Limonene
- Super Omega-3 EPA/DHA with Sesame Lignans & Olive Fruit Extract
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- Super Ubiquinol CoQ10
- Super Ubiquinol CoQ10 with BioPQQ®
- Super Ubiquinol CoQ10 with Enhanced Mitochondrial™ Support
- Theflavin Standardized Extract
- TMG Powder
- TMG Liquid Capsules

HERBAL/PHITO PRODUCTS
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- Asian Energy Boost
- Astaxanthin w/Phospholipids
- Berry Complete
- Blueberry Extract
- Blueberry Extract w/Pomegranate
- Butterbur Extract w/Standardized Rosmarinic Acid
- Calcium D-Glucarate
- Enhanced Berry Complete w/Acai
- Full-Spectrum Pomegranate™
- Grapeseed Extract with Resveratrol & Pterostilbene
- Huperzine A
- Kyolic® Garlic Formula 102 + 105
- Kyolic® Reserve
- Mega Green Tea Extract
- Mega Green Tea Extract (Decaffeinated) (also w/CoffeeGenic® Green Coffee Extract)
- Mega Lycopene Extract
- Optimized Ashwagandha Extract
- Optimized Garlic
- Pomegranate Extract
- Pycnogenol

Optimized Quercetin
- Resveratrol with Synergistic Grape-Berry Actives
- Rhodiola Extract
- Silymarin
- SODzyme™ with GliSODin®
- Stevia Extract
- Advanced Bio-Curcumin®
- with Ginger & Turmerones
- Super Bio-Curcumin®
- Super Ginkgo Extract
- Triple Action Cruciferous Vegetable Extract
- Venotenone
- Whole Grape Extract

HORMONES
- Advanced Natural Sex for Women® 50+
- 7-KETO® DHEA
- DHEA
- DHEA Complete
- GH Pituitary Support Day Formula
- GH Pituitary Support Night Formula
- Liquid Melatonin
- Melatonin
- Melatonin Timed Release
- Natural Estrogen with Pomegranate Extract
- Pregnenolone
- ProgestaCare for Women
- Super Miraforte with Standardized Lignans

IMMUNE ENHANCEMENT
- AHCC® (Active Hexose Correlated Compound)
- Black Cumin Seed Oil
- Black Cumin Seed Oil w/Bio-Curcumin®
- Buffered Vitamin C Powder
- Echinacea Extract
- FlorAssist™ Probiotic
- l26 Hyperimmune Egg
- Immune Modulator w/Tinofend®
- Immune Protect with PARACTIN™
- Immune Senescence Formula™
- Lactoferrin
- NK Cell Activator™
- Norwegian Shark Liver Oil
- Optimized Fucoidan w/Maritech® 926
- Pycnogenol® French Maritime Pine Bark Extract
- Red Yeast Rice
- Super Absorbable CoQ10™ w/d-Limonene
- Super Omega-3 EPA/DHA
- Teacrine
- Tart Cherry w/Standardized CherryPURE®
- TMG Liquid Capsules
- Theflavin Standardized Extract

INFAMMATORY REACTIONS
- Arthro-Immune Joint Support
- ArthroMax® with Theaflavins
- Boswellia
- Bromelain (Specially-coated)
- Cytokine Suppressor™ with EGCG
- DHA (Vegetarian Sourced)
- Fast Acting Joint Formula
- Ginger Force®
- Krill Healthy Joint Formula
- 5-LOX Inhibitor w/AprèsFlex®
- Mega EPA/DHA
- Mega GLA with Sesame Lignans
- MSM
- Organic Golden Flax Seed
- Serraflazyme
- SODzyme™ with GliSODin® and Wolfberry
- Super Omega-3 EPA/DHA
- Sesame Lignans & Olive Fruit Extract
- Tart Cherry w/Standardized CherryPURE®
- Zyflamend® Whole Body

LIVER HEALTH
- Branch Chain Amino Acids
- Certified Mega Lycopene Milk Thistle
- N-Acetyl Cysteine
- Liver Efficiency Formula
- European Milk Thistle
- Hepatopro
- SAMA
- Silymarin
**PRODUCTS**

**SKIN CARE**
- Advanced Lightening Cream
- Advanced Peptide Hand Therapy
- Advanced Triple Peptide Serum
- Advanced Under Eye Serum with Stem Cells
- Amber Self MicroDermAbrasion
- Anti-Aging Masque
- Anti-Glycation Serum
- Anti-Aging Rejuvenating Face Cream with Green Coffee Extract
- Corrective Clearing Mask
- DNA Repair Cream
- Essential Plant Lipids Reparative Serum
- Face Master® Platinum
- Face Rejuvenating Antioxidant Cream
- Enhanced FerriBlock® with Red Orange Complex
- Fine Line-Less
- Hair Suppress Formula
- Hyaluronic Facial Moisturizer
- Hydrating Anti-oxidant Face Mist
- Hydroderm®
- Lifting & Tightening Complex
- Lycopenic Cream
- Melatonin Cream
- Mild Facial Cleanser
- Neck Rejuvenating Antioxidant Cream
- Pigment Correcting Cream
- Ultra RejuveNight™
- Ultra RejuveNight™ w/o Progesterone
- Ultra Lip Plumper
- Ultra Wrinkle Relaxer
- Under Eye Refining Serum
- Under Eye Rescue Cream
- Vitamin C Serum
- Vitamin D Lotion
- Vitamin E Essential Cream
- Vitamin K Healing Cream
- Youth Serum

**SOY**
- Natural Estrogen w/Pomegranate
- Super Absorbable Soy Isoflavones
- Ultra Soy Extract

**SPECIAL PURPOSE FORMULA**
- AMPK Activator
- Anti-Alcohol Antioxidants w/HepatoProtection Complex
- Benfotiamine w/Thiamine
- Breast Health Formula
- Butterbur Extract w/Standardized Rosmarinic Acid
- Chlorella
- Chlophyllin
- Green Coffee Extract CoffeeGenic®

**SPORTS PERFORMANCE**
- Creatine Capsules
- DMG (N, N-dimethylglycine)
- L-Glutamine Capsules
- L-Glutamine Powder
- Whey Protein Isolate
- Whey Protein Concentrate

**VITAMINS**
- Ascorbyl Palmitate Capsules
- B12
- Beta-Carotene
- Biotin Capsules
- Buffered Vitamin C Powder
- Complete B Complex
- Effervescent Vitamin C
- Fast-C®
- Folic Acid + B12
- Gamma E Tocopherol w/Sesame Lignans
- Gamma E Tocopherol/Tocotrienols
- Inositol Capsules
- Mega Lycopene Extract
- Methylcobalamin
- MK-7
- No-Flush Niacin
- Optimized Folate
- Super Ascorbate C Capsules
- Super Ascorbate C Powder
- Super K w/Advanced K2 Complex
- Tocotrienols w/Sesame Lignans
- Vitamin B3 (Niacin) Capsules
- Vitamin B6
- Vitamin B12 Lozenges
- Vitamin C
- Vitamin D3
- Vitamin D3 w/Sea-Iodine™
- Vitamins D and K w/Sea-Iodine™
- Vitamin E
- Vitamin K2

**WEIGHT MANAGEMENT**
- Advanced Anti-Adipocyte Formula w/Meratrim® & Integra Lean®
- Advanced Natural Appetite Suppress
- CalReduce Selective Fat Binder
- CoffeeGenic® Green Coffee Extract
- 7-KETO DHEA
- DHEA® Complete
- Fucoxanthin Slim™
- Garcinia HCA
- Integra-Lean® African Mango Irvingia
- Optimized Irvingia w/Phase 3® Calorie Control Complex
- Optimized Saffron with Satiereal®
- Natural Glucose Absorption Control
- Super Citrimax®
- Super CLA Blend w/Guarana and Sesame Lignans
- Super CLA Blend w/Sesame Lignans
- WellBetX PGX® plus Mulberry
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**EXTRA 10% OFF ALL PRODUCTS DURING SUPER SALE**
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<td>CALREDUCE SELECTIVE FAT BINDER - 120 mint chewable tablets</td>
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<td>CARDIOP EAK™ w/STANDARDIZED HAWTHORN &amp; ARALUNA - 120 veg. caps</td>
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<td>CLA BLEND w/ARANNA &amp; SESAME (SUPER) - 3,000 mg, 120 softgels</td>
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<td>COGNITEX w/BRAND SHIELD - 90 softgels</td>
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<td>COGNITEX w/PREGNENOLONE &amp; BRAIN SHIELD - 90 softgels</td>
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<td>COGNITEX® BASICS - 60 softgels</td>
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**BUYERS CLUB ORDER FORM**

LIFE EXTENSION MEMBERS RECEIVE 25% OFF THE RETAIL PRICE OF ALL PRODUCTS

DEDUCT AN ADDITIONAL 10% ON ALL PRODUCTS DURING SUPER SALE

JANUARY 2015

OFFER ENDS FEBRUARY 2, 2015

To order online visit www.LifeExtension.com/SuperSale

To order online visit: www.LifeExtension.com/SuperSale

COGNIZIN® CDP CHOLINE CAPS - 250 mg, 60 veg. caps  $36.00 $27.00
Buy 4 bottles, price each  $34.00 $25.50

COMPLETE B-COMPLEX - 60 veg. caps  $10.00 $7.50
Buy 4 bottles, price each  $9.00 $6.75

COMPREHENSIVE NUTRIENT PACKS ADVANCED - 30 packs  $90.00 $67.50
Buy 4 boxes, price each  $82.00 $61.50

COOPER CAPSULES - 2 mg, 100 caps  $9.91 $7.43

COQ10 w/LIMONEN (SUPER-ABSORBABLE) - 50 mg, 60 softgels  $25.00 $18.75
Buy 4 bottles, price each  $22.00 $16.50
Buy 10 bottles, price each  $20.00 $15.00

COQ10 w/LIMONEN (SUPER-ABSORBABLE) - 100 mg, 100 softgels  $66.00 $49.50
Buy 4 bottles, price each  $60.00 $45.00
Buy 10 bottles, price each  $56.00 $42.00

COQ10 (SUPER-UBIQUINOL) - 2 mg, 100 caps  $14.00 $10.50
Buy 4 bottles, price each  $12.00 $9.00
Buy 10 bottles, price each  $10.00 $7.50

COQ10 w/ENH MITOCHONDRIAL SUPPORT™ (SUPER UBIQUINOL) - 100 mg, 60 softgels  $62.00 $46.50
Buy 4 bottles, price each  $56.00 $42.00
Buy 10 bottles, price each  $52.00 $39.00

COQ10 w/ENH MITOCHONDRIAL SUPPORT™ (SUPER UBIQUINOL) - 50 mg, 100 softgels  $58.00 $43.50
Buy 4 bottles, price each  $53.00 $39.75
Buy 10 bottles, price each  $50.00 $37.50

COQ10 w/ENH MITOCHONDRIAL SUPPORT™ (SUPER UBIQUINOL) - 50 mg, 30 softgels  $62.00 $46.50
Buy 4 bottles, price each  $56.00 $42.00
Buy 10 bottles, price each  $52.00 $39.00

COQ10 (SUPER-UBIQUINOL) - 200 mg, 30 softgels  $36.00 $27.00
Buy 4 bottles, price each  $32.00 $24.00
Buy 10 bottles, price each  $28.00 $21.00

COQ10 w/ENH MITOCHONDRIAL SUPPORT™ (SUPER UBIQUINOL) - 100 mg, 30 softgels  $39.00 $29.25
Buy 4 bottles, price each  $35.00 $26.25
Buy 10 bottles, price each  $30.00 $22.50

COSMESIS ADVANCED LIGHTENING CREAM - 1 oz jar  $65.00 $48.75
Buy 2 bottles, price each  $60.00 $45.00

COSMESIS ADVANCED PEPTIDE HAND THERAPY - 4 oz bottle  $66.00 $49.50
Buy 2 bottles, price each  $60.00 $45.00

COSMESIS ADVANCED TRIPLE PEPTIDE SERUM - 1 oz bottle  $65.00 $48.75
Buy 2 bottles, price each  $60.00 $45.00

COSMESIS ADVANCED UNDER EYE SERUM w/STEM CELLS - 33 oz  $49.00 $36.75
Buy 2 bottles, price each  $45.00 $34.50

COSMESIS AMBER SELF MICRODERMABRASION - 2 oz  $49.00 $36.75
Buy 2 jars, price each  $45.00 $34.50

COSMESIS ANTI-AGING MASK - 2 oz  $72.00 $54.00
Buy 2 bottles, price each  $66.00 $49.50

COSMESIS ANTI-AGING REJUVENATING FACE CREAM - 2 oz jar  $65.00 $48.75
Buy 2 jars, price each  $60.00 $45.00

COSMESIS ANTI-AGING REJUVENATING SCALP SERUM - 2 oz  $65.00 $48.75
Buy 2 bottles, price each  $60.00 $45.00

COSMESIS ANTI-AGING REJUVENATING FOOT CREAM - 2 oz  $45.00 $33.75
Buy 2 jars, price each  $40.00 $30.00

COSMESIS ANTI-AGING REJUVENATING SCALP SERUM - 2 oz  $46.00 $34.50
Buy 2 bottles, price each  $40.00 $30.00

COSMESIS ANTI-AGING REJUVENATING SCALP SERUM - 2 oz  $55.00 $41.25
Buy 2 bottles, price each  $50.00 $37.50

COSMESIS ANTI-AGING REJUVENATING SCALP SERUM - 2 oz  $56.00 $42.00
Buy 2 bottles, price each  $50.00 $37.50

COSMESIS ANTI-AGING REJUVENATING SCALP SERUM - 2 oz  $64.00 $47.00
Buy 2 bottles, price each  $59.00 $44.25
Buy 2 jars, price each  $51.92 $38.94

**SUB-TOTAL OF COLUMN 3**

**SUB-TOTAL OF COLUMN 4**
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<td>80101</td>
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**SUPER SALE SAVINGS ON ALL PRODUCTS**

**DEDUCT AN ADDITIONAL 10% ON ALL PRODUCTS DURING SUPER SALE**

LIFE EXTENSION MEMBERS RECEIVE 25% OFF THE RETAIL PRICE OF ALL PRODUCTS
<table>
<thead>
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<th>No.</th>
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<td>00852</td>
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<td>00544</td>
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<td>Member Each</td>
<td>Qty</td>
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<td>HCA (GARCINIA) – 90 veg. caps</td>
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<td>HYPERZINE A – 200 mcg, 60 veg caps</td>
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<td>00661</td>
<td>HYDRODERM® - 1 oz</td>
<td>79.95</td>
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<td>INNERPOWER®- - 530 grams powder</td>
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<td>JARRO-DOPHILUS EPS® - 60 veg. caps</td>
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<td>K w/ADVANCED K2 COMPLEX (SUPER) - 90 softgels</td>
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**SUB-TOTAL OF COLUMN 9**

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<td>S-LOX INHIBITOR W/APRESLEX® - 100 mg, 60 veg. caps</td>
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**SUB-TOTAL OF COLUMN 10**

To order call: 1.954.766.8433 or 1.800.544.4440

SUPER SALE SAVINGS ON ALL PRODUCTS

LIFE EXTENSION MEMBERS RECEIVE 25% OFF THE RETAIL PRICE OF ALL PRODUCTS

DEDUCT AN ADDITIONAL 10% ON ALL PRODUCTS DURING SUPER SALE
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**SUB-TOTAL OF COLUMN 11**

LIFE EXTENSION MEMBERS RECEIVE 25% OFF THE RETAIL PRICE OF ALL PRODUCTS

**DEDUCT AN ADDITIONAL 10% ON ALL PRODUCTS DURING SUPER SALE**

**SUB-TOTAL OF COLUMN 12**

OFFER ENDS FEBRUARY 2, 2015

To order online visit www.LifeExtension.com/SuperSale
### Buyers Club Order Form

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**SUB-TOTAL OF COLUMN 13**

**SUB-TOTAL OF COLUMN 14**

---

**Deduct an additional 10% on all products during Super Sale**

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**Super Sale Savings on All Products**

**To order call 1-800-544-4440**

---

**LIFE EXTENSION MEMBERS RECEIVE 25% OFF THE RETAIL PRICE OF ALL PRODUCTS**

---

**January 2015**
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<td>SODSYME® w/GLISODIN® AND WOLFBERRY - 90 veg. caps</td>
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<td>24.00</td>
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<td>SOLARSHIELD SUNGLASSES - 1 pair smoke color</td>
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**Sub-Total of Column 15**

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<td>STEVIA® ORGANIC LIQUID EXTRACT (BETTER) - 2 oz liquid</td>
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<td>SUPER ABSORBABLE SOY ISOFLAVONES - 60 veg. caps</td>
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**Sub-Total of Column 16**

**Offer Ends February 2, 2015**

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<td>VITAMIN B3 NACIN - 500 mg, 100 caps</td>
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<td>ZYFLAMEND® WHOLE BODY - 120 softgels</td>
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**SUB-TOTAL OF COLUMN 17**

NEW: 01961 ZINC ACETATE LOZENGES (ENHANCED) - 18.75 mg, 30 veg. lozenges

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SUB-TOTAL COLUMN 3
SUB-TOTAL COLUMN 4
SUB-TOTAL COLUMN 5
SUB-TOTAL COLUMN 6
SUB-TOTAL COLUMN 7
SUB-TOTAL COLUMN 8
SUB-TOTAL COLUMN 9
SUB-TOTAL COLUMN 10
SUB-TOTAL COLUMN 11
SUB-TOTAL COLUMN 12
SUB-TOTAL COLUMN 13
SUB-TOTAL COLUMN 14
SUB-TOTAL COLUMN 15
SUB-TOTAL COLUMN 16
SUB-TOTAL COLUMN 17

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Shipping

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MEMBERSHIP APPLICATION

I want to contribute to your research efforts to extend the healthy human life span. Enclosed is my first year’s membership donation of $75 to join the most elite group of longevity enthusiasts in the world. (Canadians add $7, all others outside the U.S. add $35)

Item code: MEMB1. Call for multiple year membership rates.

Name ___________________________
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☑ Check enclosed (payable to Life Extension Foundation®)
☑ Charge my cc: _______
Card # _______  Exp. _______

LIFE EXTENSION MEMBERS RECEIVE 25% OFF THE RETAIL PRICE OF ALL PRODUCTS

DEDUCT AN ADDITIONAL 10% ON ALL PRODUCTS DURING SUPER SALE
Zinc stimulates the activity of about 300 enzymes and fortifies the immune system.
Taking the best zinc lozenge is important for maintaining the body's natural defense system during the cold season—and throughout the year. Enhanced Zinc Lozenges is a special "ionic formula" that delivers on the original promise of seasonal immune support.

Immune Support For Seasonal Changes
Scientific evidence is accumulating that zinc acetate is the preferred zinc compound to provide enhanced seasonal immune support.
Zinc acetate releases 100% of its zinc as ionic zinc—positively charged zinc ions. Zinc acetate lozenges have been shown to strongly support immune function.
Life Extension Enhanced Zinc Lozenges provide zinc acetate with no other ingredients that could reduce the delivery of these immune-supportive, positively charged zinc ions. Enhanced Zinc Lozenges come in a naturally flavored peppermint lozenge.
The suggested serving size of one vegetarian lozenge of Life Extension Enhanced Zinc Lozenges provides:

Zinc (as zinc acetate) 18.75 mg

A bottle of 30 vegetarian lozenges of Life Extension Enhanced Zinc Lozenges retails for $12. If a member buys two bottles during Super Sale, the price is reduced to $5.40 per bottle.

References
For Total Body Cellular Support

Astaxanthin has long been shown to promote eye health. More recent findings indicate that this member of the carotenoid family has benefits for the entire body, including the brain, heart, skin, and immune system.

Since astaxanthin is a fat-soluble compound, it has limited assimilation into the bloodstream, with as little as 50% getting absorbed by the body.\(^1,2\)

To facilitate maximum absorption of this key nutrient, Life Extension has combined 4 mg of natural astaxanthin with a proprietary blend of 80 mg of four different phospholipids. This innovative formulation has been shown to enhance carotenoid absorption by several-fold.\(^3\)

A bottle containing 30 softgels of Astaxanthin 4 mg with Phospholipids retails for $16. If a member buys four bottles during Super Sale, the price is reduced to $9.45 per bottle.

Contains soybeans.

References

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.
SWIVEL offers a special incentive for WOMEN.

Why a Special Focus on Women? ♥

Men outnumber women throughout the various levels of the life extension community. SWIVEL would like to reach out to those women who share a serious interest in the science of extending life. And yes, men are also invited. We just want to even out the playing field.

What Are These Levels of Life Extension? ♥

1) Squaring the Curve. The standard path is to be born, enjoy a vigorous, healthy period and then start to deteriorate until death. Those seeking to square the curve wish to take advantage of evidence based medical and technological science to stay healthy and vigorous right up until the end. It’s called “Health Extension.” This is the largest level.

2) Extend the Maximum Lifespan. Currently, the maximum human life-span is about 120 years. Some individuals are going further and looking to evidence based science and technology to extend this period to 150 years or 200 years or…… Their goals vary. This is the next largest level.

3) Indefinite Lifespan. The smallest group seeks an indefinite life-span. Some call themselves immortalists. They also look to evidence based science to conquer all diseases of aging. Some have made arrangements to be cryo-preserved should they deanimate (legal death) before mankind conquers death.

Incentive for Women ♥

An extended flyer is being sent to relevant organizations. It is our hope that one or two women from each will say, “Yes, that’s me.” All women receive a 50% discount. The regular price is $800 for 8 full days. Women will be charged $400 (includes a daily buffet lunch).

Mention this LEP announcement for $100 off. ♥

Program ♥

Our program will run from 10 am to 6 pm each day and will break for a healthy buffet lunch from 1pm - 2 pm. This is Vegas and we know that you just might be up late.

Unstructured events alone do not actually lead to everyone getting to meet those with whom they might have a shared interest. Therefore, several getting acquainted exercises, introductions and breakout groups have been designed to maximize your chance of meeting the “right” date, friends and colleagues. Evenings are unstructured. We will provide announcements for those who wish to organize specific evening events. “Everyone who wants to…… meet here…… at …pm.”

SWIVEL ♥

a device joining two parts so that one or both can pivot freely

Come look around.

WHY A FULL 8 DAYS ? ♥

SWIVEL’s goal is very specific. We want to reach those individuals who identify with maximizing their healthy life-span at any level and then help them to meet each other. Community support follows.

SWIVEL wants more than brief introductions. We want enough time for you to ask YOUR questions in a no pressure environment. We want YOU to have enough time to actually get to know each other - enough time to decide if you wish to spend more time getting to know someone. We want to be effective.

Healthy life-span enthusiasts generally want to find a like minded partner.

WHY VEGAS ? ♥

Easy to reach. Lodging to fit every budget.

LODGING ♥

Our event site, The Orleans, is offering these attractive rates for single or double occupancy until 6-24-15. Resort Fee = $12.99. Taxes = 12%.

Sunday through Thursday .................. $41
Friday and Saturday ....................... $95

Search “Vegas lodging” for additional sites.

To request your Registration Form (mention this announcement for $100 off), along with more detailed information, please e-mail us at: SWIVELclub@aol.com ♥
Curcumin + Ginger

THE POWER OF CURCUMIN

HOW MUCH CURCUMIN ARE YOU ABSORBING?

Derived from the Indian spice turmeric, curcumin is acclaimed for its wide range of health-promoting effects on almost every organ system, while supporting the body’s healthy inflammatory response.

Most curcumin extracts are neither well absorbed nor well retained in the body.

Advanced Bio-Curcumin® with Ginger & Turmerones contains BCM-95®, a patented, bioenhanced preparation of curcumin that has been shown to reach up to 7 times higher concentration in the blood than standard curcumin. In addition to the benefits of BCM-95® this advanced formula provides:

- **Turmerones**: botanical compounds that remain after curcumin is extracted, enhancing curcumin absorption and increasing the amount of curcumin inside cells.
- **Ginger**: a close relative of curcumin with overlapping, complementary health benefits.
- **Phospholipids**: an emulsifying molecule that greatly enhances absorption.

The suggested daily dosage of a softgel of Advanced Bio-Curcumin® with Ginger & Turmerones provides:

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<th>Component</th>
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<tr>
<td>Turmeric Phospholipid Blend</td>
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<tr>
<td>BCM-95® Bio-Curcumin Turmeric 25:1 extract (rhizome)</td>
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<tr>
<td>Total curcuminoids complex with essential oils (380 mg)</td>
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<tr>
<td>Turmeric oil (rhizome) (providing 60 mg total turmerones)</td>
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<tr>
<td>Phospholipids</td>
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<tr>
<td>Ginger CO₂ extract (root) (providing 60 mg gingerols)</td>
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Each softgel of Advanced Bio-Curcumin® with Ginger & Turmerones provides 400 mg of BCM-95® Super Bio-Curcumin, plus an array of turmerones and phospholipids.

A bottle of 30 softgels of Advanced Bio-Curcumin® with Ginger & Turmerones retails for $30. If a member buys four bottles during Super Sale, the price is reduced to $18.23 per bottle.

Contains soybeans.

References

Bio-Curcumin® and BCM-95® are registered trademarks of Dolcas®-Biotech, LLC.

Caution: Do not take if you have gallbladder problems or gallstones. If you are taking anticoagulant or antiplatelet medications, or have a bleeding disorder, contact your healthcare practitioner before taking this product.

To order Life Extension® Advanced Bio-Curcumin® with Ginger & Turmerones, call 1-800-544-4440 or visit www.LifeExtension.com

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66 NOVEL FORM OF VITAMIN B3 “TURNS OFF” AGING GENES
The fatigue that accompanies aging may partially be caused by reduced levels of NAD+. Boosting NAD+ can activate anti-aging sirtuin enzymes and increase DNA repair.

7 REVERSE AGE-RELATED IMMUNE DECLINE
Researchers have identified specific immune components that decline with aging. The exciting news is that natural ways have been discovered to reverse this trend and restore more youthful immune profiles in maturing individuals.

26 A VIRUS THAT ACCELERATES IMMUNE SENECEENCE
Approximately 60 to 90% of adults are infected with cytomegalovirus, which can result in shortened life span and depletion of vital naïve immune cells. Find out how to suppress chronic infection of this insidious virus and offset its age-accelerating effects.

40 BOOSTING IMMUNE FUNCTION IMPROVES LONGEVITY
Reversing immune decline increases the production of naïve T-cells necessary to attack invaders such as bacteria, viruses, and cancer cells. Scientists have identified two botanicals that help restore our aging immune systems, including production of naïve T-cells.

52 ACTIVATE NATURAL KILLER CELLS AGAINST WINTER INFECTIONS
Natural killer (NK) cells are our first line of defense against infections, especially wintertime viruses. A natural compound from enzymatically modified rice bran increases NK cell activity in circulating blood cells by up to 84%.

76 AMERICAN ACADEMY OF ANTI-AGING MEDICINE CONFERENCE
This report highlights presentations from the world’s largest anti-aging conference, including the benefits of longer telomeres, strategies for detoxification, and more.