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## Acetylcholine Enhancement: Galantamine and DMAE's Cognitive Supportive Role

by Ward Dean, MD

Cognitive function is controlled by the central nervous system, which in turn is controlled by the cholinergic system, a system of cells that produce and/or are stimulated by the neurotransmitter, acetylcholine, a neurotransmitter that plays an integral role in learning and memory. Receptors respond to acetylcholine to facilitate intracellular communication, memory processing and higher cognitive functions. Acetylcholine is rapidly broken down by an enzyme, acetylcholinesterase (AChE), and made available to be recycled.

Diminished cholinergic functioning, a biomarker of normal aging, is especially severe in cases involving dementia. In Alzheimer's for example, amyloid plaque

deposits in key components of the cholinergic system cause a drastic decline in acetylcholine levels. To make matters worse, already reduced acetylcholine levels continue to be degraded by AChE, further impairing memory and eroding cognitive ability.

Acetylcholinesterase inhibitors that suppress acetylcholinesterase to prevent it from degrading acetylcholine allow the neurotransmitter to persist in the synaptic cleft for a longer period of time, enhancing cognitive function.

Galantamine, a natural compound derived from the common snowdrop (*Galanthus nivalis*), is a natural acetyl-

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## Andropause and Menopause: Natural Strategies to Rebalance Hormonal Health

by Chris D. Meletis, ND

Aging is associated with progressive alterations in the hormonal environment for both men and women. In men this is called andropause and in women it's called menopause. These changes are readily recognized in women with cessation of menses and often the onset of hot flashes, vaginal dryness and a myriad of other hormone-induced symptoms including anxiety, depression and change in muscle mass. In men, without the overt cessation of a monthly cycle, these changes can be much more difficult to identify. All too often both sexes quietly and unnecessarily accept these changes as "just getting

old." Yet, no one should passively accept a decrease in energy, diminished sense of wellness and lack of zeal for life.

With the stresses of modern living, including external hormonal exposures from diet and environmental chemicals, the human body no longer passes into this hormonal state with the ease of past generations. The fact that indigenous cultures around the world do not suffer symptoms of andropause and menopause to the extent that we in industrialized nations do, further support that external hormonal factors

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# Acetylcholine

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cholinesterase inhibitor. It also potentiates cholinergic receptors.<sup>1</sup>

Galantamine is extremely well studied, and in the last six months, new research has accumulated to expand upon the already extensive evidence in support of galantamine's cognitive-enhancing abilities. This article will review those new studies and discuss another natural agent, Dimethylaminoethanol (DMAE) that can be used in conjunction with galantamine to enhance cognitive abilities.

## Galantamine and Cognitive Enhancement

One of the most recent studies on galantamine demonstrated that it does act as an acetylcholinesterase inhibitor in Alzheimer's patients. The researchers investigated galantamine's effects in 18 patients with mild Alzheimer's disease. The first three months of the study had a randomized double-blind placebo-controlled design, during which 12 patients received galantamine (16-24 mg per day) and six patients received a placebo. This was followed by nine months' galantamine treatment in all patients. In patients on galantamine, acetylcholinesterase inhibition was 30-36 percent in the cerebrospinal fluid, which correlated well with the in vivo acetylcholinesterase inhibition in the brain. No significant acetylcholinesterase inhibition was observed in the placebo

group. The acetylcholinesterase inhibition that occurred after galantamine positively correlated with the patients' performance on cognitive tests.<sup>2</sup>

Brodaty et. al. recently conducted another human trial of galantamine in Alzheimer's patients. In this prospective, open-label, observational study, 345 subjects with mild to moderately severe dementia of the Alzheimer's type were recruited from 48 hospitals in Australia. Subjects received galantamine for six months in a clinical practice setting. The participants were assessed at baseline and three and six months after starting galan-

***“Acetylcholinesterase inhibition that occurs after galantamine positively correlates with patients’ performance on cognitive tests.”***

tamine. The researchers used a number of tests to determine the subject's cognitive function, including the Mini-Mental State Examination (MMSE), the Clinician's Interview-Based Impression of Change plus Caregiver Input (CIBIC-plus) and the Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-cog). Researchers also used an abridged Instrumental Activities of Daily Living (IADL) questionnaire that included questions on using the telephone, ability to travel more than 1 km outside the home, taking medications and managing money, and an 11-item behavior assessment scale that measured aggression, sleep disturbance, disinhibition, personality changes, irritability, depression, agitation, apathy, inertia, hallucinations and aberrant motor behavior.

Of the 345 subjects who were enrolled in the study, 229 completed the baseline and three- and six-month visits. At 6 months of galantamine usage, most subjects (70 percent) showed an increase in MMSE score. Of the 21 patients who were assessed

using the Alzheimer's Disease Assessment Scale-cognitive subscale, 18 (86 percent) demonstrated a decrease in the ADAS-cog score, reflecting an improvement in cognition. Most subjects (86 percent) were considered responders according to the Clinician's Interview-Based Impression of Change plus Caregiver Input score, with 65 percent showing some improvement over six months of galantamine use. No deterioration in Instrumental Activities of Daily Living or behavior assessments occurred in the majority of subjects over six months.<sup>3</sup>

According to the researchers, “In a clinical practice setting, the majority of subjects receiving galantamine who completed the study maintained their ratings of cognition, function, behaviour or global assessment over the 6-month period.”

Due to the promising research that exists supporting galantamine's ability to improve cognitive function, researchers have begun to delve more deeply into exactly how galantamine might exert its effects. In a recent animal study, the scientists noted that rodents given galantamine experienced an increase in extracellular levels of dopamine, which is the immediate precursor in norepinephrine synthesis. Norepinephrine is a neurotransmitter and a disturbance in its metabolism at important brain sites has been associated with cognitive disorders.

In the above study, researchers used a mouse model of Alzheimer's disease to investigate galantamine's effects. They injected mice with beta amyloid, a protein implicated in Alzheimer's disease. Compared to saline injected mice, animals injected with the amyloid protein could not discriminate between new and familiar objects in the novel object recognition test and exhibited less freezing response in the fear-conditioning tasks, suggesting the amyloid protein induced cognitive impairment. When these animals were given galantamine, it improved the beta amyloid induced cognitive impairment in the novel object recognition and fear-conditioning tasks. Galantamine also significantly increased the extracellular dopamine release in the hippocampus of the animals. However, when the animals were given galantamine along with agents that block dopamine, the same improvements were not noted.

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The study authors noted that this is the first in vivo evidence that galantamine augments dopaminergic neurotransmission within the hippocampus by enhancing the activity of acetylcholine receptors.<sup>4</sup>

### Smoking Cessation

One of the most interesting new studies on galantamine investigated its effects in smoking cessation. Researchers studied whether galantamine reduces smoking by performing a 24-week randomized, placebo-controlled, multicenter clinical trial in 114 recently detoxified alcohol-dependent patients. They included all study subjects irrespective of an intention or motivation to abstain from nicotine. Specific treatment for cessation or reduction of smoking was not provided. The scientists determined smoking behavior through patients' diaries and measured the nicotine metabolite cotinine to verify the number of smoked cigarettes. Fifty-six of the smokers were randomized to receive galantamine while 58 received a placebo for 12 weeks. Smoking behavior did not differ between both groups at baseline.

Analysis revealed significant differences between groups, with a 20 percent lower cumulative number of smoked cigarettes and a 15 percent lower number of smoking days in the galantamine group compared to placebo. The average number of smoked cigarettes per smoking day as well as the cotinine values decreased about 10 percent in the galantamine group.<sup>5</sup>

According to the researchers, "Our tentative data indicate that galantamine reduces smoking behavior even without any additional specific intervention. We suggest introducing the term 'substitution therapy' into the treatment of smoking. This result could open up a new treatment approach for groups of patients which usually have a low motivation for change."

### Autism

Because abnormalities in acetylcholine metabolism have been associated with autism, scientists recently investigated the use of galantamine in children with this disorder. Thirteen medication-free children with autism (mean age, 8.8 years) participated in a 12-week, open-label trial of galantamine. Patients were rated monthly by parents on the Aberrant Behavior Checklist (ABC) and the Conners' Parent Rating Scale-Revised, and by a physician using the

Children's Psychiatric Rating Scale and the Clinical Global Impressions scale.

Autistic children using galantamine showed a significant reduction in parent-rated irritability and social withdrawal on the ABC as well as significant improvements in emotional lability and inattention on the Conners' Parent Rating Scale-Revised. Similarly, clinician ratings showed reductions in the anger subscale of the Children's Psychiatric Rating Scale. Eight of 13 participants were rated as responders on the basis of their improvement scores on the Clinical Global Impressions scale. Overall, galantamine was well-tolerated, with no significant adverse effects apart from headaches in one patient.<sup>6</sup>

"In this open trial," the researchers wrote, "galantamine was well-tolerated and appeared to be beneficial for the treatment of interfering behaviors in children with autism, particularly aggression, behavioral dyscontrol, and inattention. Further controlled trials are warranted."

### DMAE and Cognitive Enhancement

Along with galantamine, DMAE is important to include in a list of cognitive-enhancing substances. Dimethylaminoethanol (DMAE) is a naturally-occurring, mild cerebral stimulant nutrient found in such "brain" foods as anchovies and sardines.

Like galantamine, DMAE influences acetylcholine metabolism (Fig. 1). It has long been known to stimulate the production of choline, which in turn allows the brain to optimize production of acetylcholine.<sup>7-9</sup> However, Professor Imre Zs.-Nagy believes that enhanced acetylcholine is not the only explanation for DMAE's effect, since he believes that a choline-rich diet alone should have the same acetylcholine-increasing effect, which he believes is not the case. Zs.-Nagy proposes that other mechanisms of DMAE include its being a free radical scavenger (with particular ability to protect cellular membranes); cross-linkage inhibitor; and spin trapper (a type of free radical scavenger).<sup>10</sup> In addition, Dr. Richard Hochschild proposed that DMAE's principal anti-aging mechanism is that of acting as a "cell membrane fluidizer."<sup>11</sup>

DMAE has been used for years to improve behavioral disorders in children,

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## The President's Desk

### Protecting Hormonal Health

Recently, I became concerned about another attack on our health freedom. I am referring to an American Medical Association (AMA) resolution concerning compounded, bioidentical hormones, which threatens our ability to obtain safe, beneficial natural hormones. The resolution asks the FDA to institute regulatory changes that may limit the ability to obtain prescribed compounded or even off-label medicines.

Healthcare professionals and patients should be concerned about the AMA's new resolution. Currently, state pharmacy boards regulate pharmacies, including compounding pharmacies. Virtually every major healthcare organization and agency recognizes that customized, compounded medicines are a vital part of healthcare, providing a necessary alternative to one-size-fits-all medicines. However, if the FDA were to intervene, it could assert that compounded medicines are illegal, which puts patients who rely on compounded medicines at risk and interferes with clinicians' ability to treat patients. Furthermore, the resolution fails to recognize state pharmacy boards should and do play an active role in regulating compounded hormones. This is inconsistent with AMA's longstanding policy that states have a primary role to play and sets a dangerous precedent.

The AMA has long supported giving doctors broad discretion to determine what medical and pharmaceutical treatments patients need. For example, millions of Americans rely on lawful and medically appropriate "off-label" and compounded medications for their health, even though they're not "FDA-approved." If the FDA extends its reach into these areas of physician discretion, what begins as restrictions on compounding may lead to comparable limitations on the availability of medicines for off-label uses.

Finally, the organizations that introduced this resolution—The Endocrine Society, the American Association of Clinical Endocrinologists and the American Society for Reproductive Medicine—have received at least several hundred thousand dollars in funding from Wyeth, the manufacturer of synthetic hormone replacement medicines.

I urge everyone to take action against the AMA resolution by visiting <https://secure2.convio.net/iacprx/site/Advocacy?pagename=homepage&page=UserAction&id=143>. At this site, you can send an email to the CEO of the American Medical Association.

  
Robert Watson  
President/CEO

# Acetylcholine

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and results in positive effects on intelligence and grades as well. DMAE produces a mild stimulant effect, which develops slowly over a period of several weeks. There is no drug-like letdown or depression if it is discontinued.<sup>12</sup>

In 1958, Dr. Leon Oettinger, Jr., found that DMAE.<sup>13</sup>

- Accelerated mental processes
- Improved concentration
- Stopped early morning “fogginess”
- Relieved lassitude and mild depression
- Was useful in schizophrenia of long duration (with prolonged treatment)
- Decreased irritability and reduced overactivity, leading to a much better overall social adaptation and improved scholastic functioning
- Increased attention
- Did not cause drowsiness
- Improved IQ.

Furthermore, Dr. Oettinger found that DMAE had numerous advantages over the amphetamines (like Ritalin) in that there were no effects on heart rate or blood pressure and no induced “jitteriness.” Instead of causing anorexia (loss of appetite) like the amphetamines, he found that DMAE actually improved appetite in many patients and caused no interference with sleep. In fact, he found that DMAE actually reduced sleep requirements. Dr. Oettinger concluded that DMAE “was a most useful tool in the handling of the child with behavioral problems.”

In 1960, Dr. Stanley Geller reported on a double-blind study of 75 children, that DMAE in doses of 50 mg twice daily resulted in improved functioning capacity, puzzle-solving ability and organization of activity.<sup>14</sup>

In another double-blind study of fifty children who had been diagnosed as suffering from “hyperkinetic syndrome,” DMAE was administered in doses up to 500 mg/day (300 mg in the morning; another 200 mg at lunch). The authors concluded that DMAE, “when administered at doses of 300 to 500 mg per day for 12 weeks to moderately disturbed hyperkinetic children (six to 12 years of age) produces greater overall improvement in comparison to patients similarly treated with a placebo.”<sup>15</sup>

Although most of the human studies involving DMAE and cognitive enhancement seem to have been conducted in the 1950s and 1960s, a recent animal study confirmed the memory/intelligence-improving effects of DMAE. Animals fed DMAE were better able to negotiate a maze compared to untreated animals.<sup>16</sup>

## Chronic Fatigue and Depression

DMAE has been demonstrated to be useful in chronic fatigue as well as in depression in children.<sup>17</sup> It also normalizes brain function and mood.<sup>18</sup>

A recent study in Germany evaluated the effects of DMAE in subjects suffering from borderline emotional disturbance and depression, using a combination of EEG (electroencephalogram) and psychometric testing. The scientists found that DMAE use resulted in decreased theta and alpha waves, characteristic of increased

vigilance and attention. In addition, the subjects reported increased activity and better mood. The authors concluded that DMAE induces a psychophysiological state of enhanced well being as corroborated by mood analysis and brain electrical activity.<sup>19</sup>

## Parkinson’s

DMAE improves movement disorders and prevents adverse effects of L-Dopa in Parkinsonism. In 1974, Dr. Edith Miller added DMAE in doses ranging from 300 to 900 mg per day to the regimen of Parkinson’s patients, who had begun to exhibit adverse effects from high dosages of L-Dopa (L-3, 4-dihydroxyphenylalanine, administered to treat Parkinson’s Disease). DMAE administration resulted in a complete resolution of the L-Dopa-induced abnormal movements (diskenesias) in a majority of the patients.<sup>20</sup>

Dr. Miller concluded that “DMAE seems to be the first effective measure to combat L-Dopa-induced dyskinesias safely and effectively without interfering with the beneficial effects of L-Dopa therapy.” Studies in an animal model subsequently produced similar results.<sup>21</sup> DMAE also has been shown in humans to reduce other involuntary movement disorders, including benign essential tremor and even blepharospasm (eyelid twitching). Use of DMAE resulted in improvement in all symptoms, with the exception of those suffering from Huntington’s chorea.<sup>22</sup>

## Age Spots

One of the most dramatic and well-documented effects of DMAE is its ability to inhibit the formation of aging pigment

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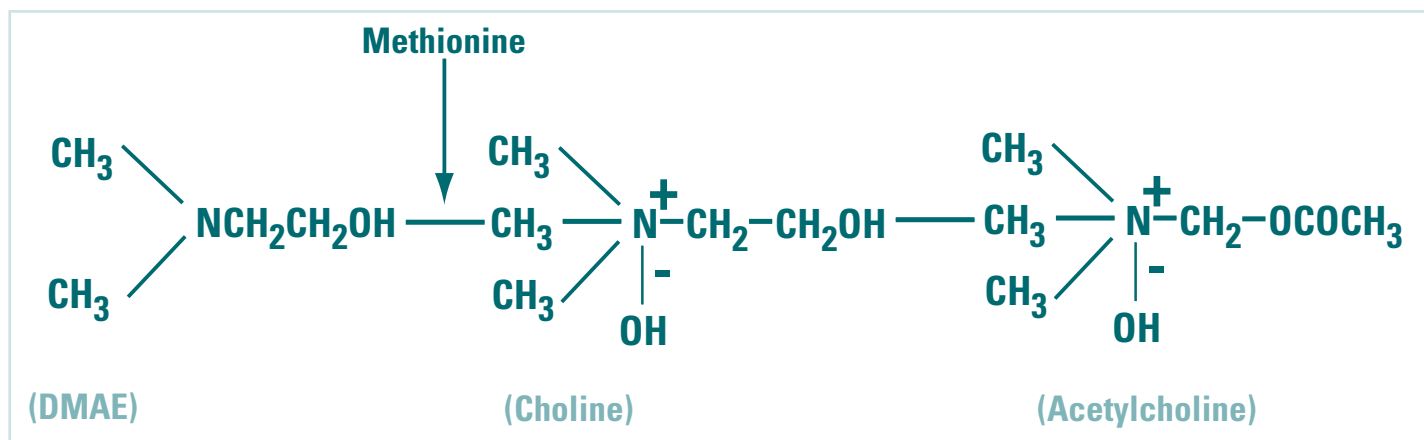


Figure 1. Chemical conversion of DMAE to choline and acetylcholine.

# CoQ10-H<sub>2</sub><sup>TM</sup>: An Important Constituent of an Over-40 Supplement Regimen

by Jeffrey Reinhardt, MSc

In the January and February issues of *Vitamin Research News*, I presented an important new form of an antioxidant cofactor known as CoQ10-H<sub>2</sub><sup>TM</sup> or ubiquinol. As discussed, CoQ10-H<sub>2</sub><sup>TM</sup>, the reduced form of CoQ10, offers a greater degree of bioavailability than the previously available form of CoQ10, known as ubiquinone. In this article, I present an interview with an expert on Coenzyme Q10 (CoQ10) wherein we explore why this new form of CoQ10 is important for anyone over the age of 40 as well as anyone facing a chronic health condition.

It was my privilege to speak with Robert J. Barry, Ph.D., a former Principle Advisor for the National Institute of Health and a preeminent scientific authority on CoQ10, who is currently in charge of Scientific Affairs, Research and New Product Development at Kaneka Nutrients, L.P., the world's leading supplier of CoQ10. Dr. Barry brings more than 18 years of strategic technical development and commercial translation of scientific products, analytical services, drug development and pre-clinical evaluation systems to his position.

In our conversation, Dr. Barry explained how to choose between the various forms of CoQ10. He also discussed the proper dosage for anyone interested in maximizing his or her cardiovascular health, cognitive functions or mitochondrial health and energy production.

**JR: Several of the recent articles on ubiquinol (reduced form CoQ10) indicate that it is the most active form and that ubiquinone (oxidized form CoQ10) is the "inactive form." Is this correct?**

**Dr. Barry:** The correct answer is that they are both metabolically active. All forms of CoQ10 are active redox cofactors and play important metabolic roles in their interconversion from one form to another. Even though ubiquinol is essential for the maintenance of energy, homeostasis, cell growth, development and viability, all CoQ10 forms are active and play specific roles in targeted areas. Likewise, the

importance of CoQ10 (ubiquinone) should not be disqualified; it has nearly 30 years of research and clinical evaluation demonstrating its considerable health benefits.

**JR: If each form of CoQ10 is beneficial, how do individuals decide which CoQ10 form is right for them?**

**Dr. Barry:** Good question. This is the short answer and not cast in stone; if you are young and healthy, and up to the age of roughly 40 to 45, you would probably want to consider ubiquinone (oxidized CoQ10). If you are older or a baby-boomer and/or are experiencing a chronic disease, or are compromised by excessive oxidative stress, then you may want to consider ubiquinol (reduced form CoQ10).

As a healthy twenty year old you readily biosynthesize and reduce all the CoQ10 you need. In fact, in a healthy individual the predominant form of CoQ10 in the plasma and tissues is the reduced form. This reduced form (ubiquinol) is a very powerful lipid-soluble antioxidant which is readily converted from the oxidized form of CoQ10 (ubiquinone).

As we get older, our bodies' ability to produce and metabolize CoQ10 declines. There are a number of reasons for this decline, including increased metabolic demand, diseases, insufficient dietary CoQ10 intake, deficiency of precursors and enzymes required for its biosynthesis, gene mutations, and oxidative stress. Some reports say this decrease in CoQ10 becomes apparent around 40 years of age; however, other reports say that CoQ10 begins to diminish as early as 20 years of age, with a slow but continuous decline thereafter. The result is less cellular energy (ATP production), slower conversion of CoQ10 to the reduced form and, consequently, a reduced protection against oxidative insult.

Ubiquinol provides a strong first stage defense against cellular oxidative stress and needs to be replenished or supplemented to maintain optimum health.

Of course these are general guidelines. Which form of CoQ10 will work best for each individual depends on many variables

including their state of health, age, etc. I recommend that each person consult with their healthcare provider in order to make the best decision.

**JR: What about dosage levels for the new ubiquinol (reduced form CoQ10)?**

**Dr. Barry:** Again this may vary and you should always consult with your healthcare provider, but a general rule may be as follows: If you are older, have a chronic disease, and/or suffer from excessive oxidative stress, and you are looking to maintain optimum health, you may want to start at 200 mg to 300 mg per day. Studies show that the CoQ10 plasma levels plateau after about two to three weeks at this dose. After that, 50 mg to 100 mg per day may be a good maintenance dose.

**JR: Thank you for taking the time to discuss these scientific advances. Do you have any parting thoughts?**

**Dr. Barry:** It is very important to note that CoQ10 concentrations in the body decrease as we age. This decline in CoQ10 is associated with the aging process and many age-related conditions, such as cardiovascular disease, neurodegenerative disease, cancer, diabetes, fatigue and the reductions in stamina and energy often associated with getting older. CoQ10 supplementation replenishes diminished levels of this important antioxidant cofactor, fostering a strong protective defense against oxidative stress and age-related diseases.

Both ubiquinone (oxidized form CoQ10) and ubiquinol (reduced form CoQ10) are critically important nutrients that should be considered seriously for optimum health, longevity and vitality.

## CATALOG CORRECTION

Please note on page 39 of the 2007 catalog there is an error. L-Theanine is a 90 count bottle not a 180 count. We apologize for any confusion this may have caused. It is correctly listed on the newsletter price list.

# Andropause/ Menopause

Continued from front page

are playing a role in this natural transition. Furthermore, many experts propose that those living in western society suffer from a lack of the adrenal gland reserves that sustain optimal wellness after gonadal (ovary/testes) hormone transitions.

## Andropause

Over 50 years ago the progressive decline in androgen production was well documented in the medical literature. This decline in testosterone commonly referred to as andropause, actually begins often in the early 30s and eventually hits a crescendo when symptoms are unmistakable. (Table 1.)

United States demographics reflect a growth in the aging population with currently greater than 35 million people over the age of 65 years, and this group will grow to 70 million by the year 2030.<sup>1</sup> Furthermore the average life expectancy is increasing. At age 65, the mean life expectancy for men is 15.2 years and 18.8 years for women.<sup>2</sup> These numbers reflect the expectancy for the *average* American without a focus on those individuals actively pursuing health, who should very well expect even greater life expectancy with a higher quality of life.

Progressive decline in hypothalamic/pituitary/gonadal function in men starting at age 30 is well documented with a free testosterone decline of 1 percent per year. After age 60, 25 percent of men are clinically overtly hypogonadal. Overt testosterone deficiency occurs in about 24 percent of men aged 50-60 years and 40 percent in men aged 60-80.<sup>3</sup> Yet it's important to realize that subclinically low testosterone levels are likely prevalent in nearly double these very conservative estimates.

In my clinical practice I recommend that any man age 30 or older with one or more symptoms listed in Table 1 have their testosterone and DHEA levels tested through salivary hormone tests. I routinely also recommend having progesterone and estradiol levels measured in men since these levels can significantly alter the effects and availability of androgen present. Men should measure their hormone levels between

8:00 and 9:00 AM since testosterone levels are at their peak in the morning.

Several approaches are routinely taken to increase testosterone levels and they include supplementing with a testosterone prescription. DHEA use is another popular non-prescription approach as is the use of a combination of herbals outlined below, which are designed to increase "free testosterone," the most bioactive form of androgen.

## Balancing Male Hormones

The goal is typically two fold: increase androgens while protecting the prostate and other tissues from excess exposure to estrogen that can result from the aromatase activity that increases with aging in men. In particular fat cells are "hot spots" for aromatase activity, where this enzyme converts androgens to estrogen.<sup>4</sup> In general, male estrogen levels increase with age, at testosterone's expense. Estrogen also tends to decrease testosterone production. Furthermore, SHBG (sex hormone binding globulin) increases with age, binding up more free testosterone.

*Eurycoma longifolia jack* extract, used in Southeast Asia for centuries, has testosterone-like actions in animal studies, and may increase testosterone levels.<sup>5,6,7</sup> Clinical response in men using *Eurycoma longifolia jack* extract have reported laboratory-tested increases in their free testosterone levels of 50 to 300 percent over several to six months' use. Further research documenting this effect shall further elucidate efficacy.

Stinging nettle root extract contains compounds that bind to SHBG, reducing the binding of testosterone to SHBG, and the binding of SHBG to prostate tissue.<sup>8,9</sup> Beta sitosterol has been shown to inhibit 5 alpha-reductase, which converts testosterone to 5 hydroxytestosterone (5HT) an undesirable metabolite of testosterone associated with benign prostatic hypertrophy.<sup>10,11,12</sup> Myricetin, a flavonoid related to quercetin, which possesses greater bioavailability than quercetin, has also been shown to inhibit 5 alpha-reductase and 5HT activity.<sup>13</sup>

Luteolin has been shown in human and animal studies to have excellent absorption and bioavailability, and to exert powerful protective effects, even at low doses. It appears superior to chrysin and other aromatase inhibitors.<sup>14-16</sup>

## Symptoms of Andropause

- Lethargy or decreased energy
- Decreased libido or interest in sex
- Decreased Concentration
- Feeling Overwhelmed
- Erectile dysfunction with Muscle weakness and aches
- Inability to sleep
- Hot flashes
- Night sweats
- Depression
- Infertility
- Thinning of bones (Osteoporosis)

Table 1.

Another tool is progesterone, a hormone produced in the male adrenal and testicular tissue that drops with aging. Further exacerbating natural progesterone decline is severe and prolonged stress since the stress hormone cortisol is made from progesterone as are testosterone, estrogen, aldosterone and other steroid hormones.<sup>17</sup>

Progesterone inhibits testosterone's conversion to DHT.<sup>18</sup> DHT is a far more potent stimulant of prostate cell growth than testosterone, whereas testosterone and progesterone stimulate the activity of a protective gene called "p53."<sup>18</sup> The products of this gene activation are anti-cancer, and promote healthy apoptosis.<sup>19</sup> Apoptosis is a "programmed cell suicide" that plays a key role in preventing cellular overgrowth (e.g., BPH) and cancer. Estrogen, on the other hand, activates a gene called "bcl2."<sup>24</sup> Bcl2 products inhibit healthy apoptosis.<sup>19</sup>

I share with my male patients that when diagnosed with low testosterone levels, any benefits from either hormonal or nutritional supplementation may take a month or more to manifest. Regardless, retesting testosterone, progesterone and estrogen after initiating a hormonal support regimen ensures that individuals have achieved the proper hormonal balance and that excess estrogen levels are not created as a result of therapy.

## Menopause

Menopause is marked officially with the cessation of menses. Estrogen levels diminish by at least 40-60 percent, and progesterone drops precipitously. The median age for onset of perimenopause, when the initial hormonal decline begins, is 47.5 years, yet can occur significantly earlier in

some individuals. Full-fledged non-surgical menopause occurs at the average age of 51.4 years in Western women. Symptoms that can accompany menopause include those in Table 2. Noteworthy is that sleep apnea, a severe case of nighttime breathing disturbance that claims 38,000 Americans each year, rises significantly during menopause. Thus it is important to evaluate symptoms of fatigue, restless sleep, heart palpitations, increase in blood pressure and dry mouth in the morning as a potential clue to a sleep apnea diagnosis.

### Balancing Female Hormones

The goal of menopausal supplementation is to support estrogen and progesterone levels while minimizing symptoms associated with this phase. In practice there are countless menopausal support approaches,

Menopausal Symptoms
• Insomnia
• Apnea
• Mild to moderate depression
• Slowed Metabolism and increased chance for weight gain
• Joint pain and muscle pain
• Increased osteoporosis
• Water retention (edema)
• Heart palpitations
• Increased bladder infection risk
• Headaches
• Vaginal dryness
• Loss of collagen and increased skin wrinkling
• Increased sweating

Table 2.

yet the following are routinely associated with favorable clinical response.

Since the mid-1950s, black cohosh has been used by over 1.5 million European women for menopausal problems. Relief of symptoms has been documented to be comparable to that obtained from Hormone Replacement Therapy (HRT), but without the harmful side effects.<sup>20</sup> Growing evidence has shown that black cohosh can confer significant relief from common menopausal symptoms such as hot flashes and night sweats.<sup>21</sup>

Genistein is the most extensively studied isoflavone phytoestrogen. Studies have shown that genistein may reduce the symptoms of menopause, prevent bone loss, and

### Functions of Progesterone

- Builds bones and protects against osteoporosis
- Helps burn fat for energy
- Maintains the uterine lining
- Necessary for the fetus to survive until birth
- Acts as a natural diuretic
- Maintains thyroid hormone action for thermogenesis (fat burning)
- Normalizes blood clotting
- Restores and maintains sex drive
- Helps prevent breast and endometrial cancer

Table 3.

possibly provide a safe alternative for prescription estrogens.<sup>22</sup>

Tribulus has been found to improve libido and alleviate hot flashes, depression and emotional lability. Use of tribulus for several months has been reported to decrease the intensity and occurrences of hot flashes, insomnia, irritability, depression, apathy and loss of sexual interest. Two thirds of the women tested reported increased sex drive after treatment with tribulus. An active preparation is obtained from the above-ground part of the plant that contains steroid saponins (not less than 45 percent).<sup>23-24</sup>

With the cessation of progesterone production in the ovaries, estrogen dominance is a serious concern for the menopausal woman. The unopposed estrogen can contribute to weight gain, cancer and changes in sense of psychological wellness. The benefits of progesterone are noted in Table 3.<sup>25-29</sup>

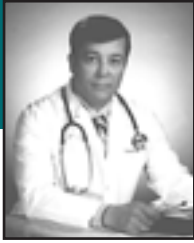
### Summary

Effectively supporting individuals who are undergoing andropause or menopause requires sustaining healthy hormone levels. At the same time, men and women entering either of these life phases should strive to prevent excess detrimental metabolites—in particular estrogens in both sexes and detrimental testosterone forms in men—in order to achieve healthy aging and maximal quality of life.

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# CUSTOMERS' CORNER

by Ward Dean, MD  
Medical Director

## High Bilirubin

Dear Dr. Dean,

I have high bilirubin at 1.8 mg/dL, which is above normal. As a result I have pruritic itch. I will appreciate if you can advise what supplement will help me reduce the bilirubin.

Thanks,  
Mr. F.

Dear Mr. F.,

You might consider *HepatoGen™*. *Hepato-Gen* is designed to optimize liver function, and may help to normalize your bilirubin. I would also like to know if any of your other liver values are abnormal.

Let me know how you do.

Ward Dean, M.D.

## Depression, Panic Attacks

Dear Dr. Dean,

I just purchased two bottles of *Lithium Orotate*. I have been taking another brand of lithium but after reading some of the letters I thought perhaps yours was a better quality. I have been taking four *Lithium Orotate* capsules per day for about ten days now and feel no different. I have been struggling with depression and panic attacks. It seems the depression sets off the attacks so that is what I am working on.

I have tried just about every drug out there and *Prozac®* seems to work the best for depression but not the panic (in fact it makes the panic worse). So I am trying this route.

My main problem with panic attacks is that they come while driving. When needed I take a *Xanax®*. I was thinking about adding *5-HTP* (200 mg at night) with the *Lithium Orotate* and raising the *Lithium* dose to 6 per day. Can I take the *Xanax* and the *5-HTP*? I'd rather not take the *Xanax* and hope once (and if) any of these products kick in I won't have to. I am pretty desperate right now and am just looking for some advice.

Mr. G.

Dear Mr. G.,

I agree with your plan to increase your dosage of *Lithium Orotate*. You may require a higher dosage. Six to 8 caps per day may help. Your plan to try adding *5-HTP* may also help. Of course, there is no contraindication, per se, of combining *5-HTP* with *Xanax*, but taking *Xanax* to prevent panic attacks when driving is not recommended.

*L-Theanine*, *Allay™*, or *Valerian Extract* may all help with your panic attacks, as they are all helpful in alleviating anxiety.

Hope these suggestions help.

Ward Dean, M.D.

## Lowering Testosterone

Dear Dr. Dean,

How can a woman lower her testosterone levels?

Mrs. R.

Dear Mrs. R.,

Usually, in women, elevated testosterone is due to abnormal conversion of adrenal hormones to androgenic hormones. To block this from happening you can try the drug *Metformin*. Or, you might try *GluControl™*, which would likely be similarly effective in preventing this conversion. In addition, to reduce adrenal hormone production, I recommend *AdaptaPhase® I*.

Finally, do not take *DHEA* or *Pregnenolone*, as both of these may increase testosterone in sensitive women.

Ward Dean, M.D.

## Vitamin E

Dear Dr. Dean,

Thank you for your help last year in establishing an Alzheimer's disease protocol for my mother and me. Your recommended supplementation regimen, in combination with her two medications, have allowed her to leave her bed, go shopping for the first time in two years, and take over paying the bills, her favorite occupation.

*The New England Journal of Medicine*

published an article about the benefits of *Vitamin E*. How does one best get a mix of the different *Vitamin E* forms (alpha, gamma, levo-, dextro-, and so forth), since no one probably knows which types are useful? Does too much of one type cause a shortfall of the others by crowding?

Thank you,  
Dr. D.

Dear Dr. D.,

*E Team* may be what you are looking for, as it contains what we believe is the most physiologic balance of tocopherols.

Ward Dean, M.D.

## Pregnenolone and Itching Skin

Dear Dr. Dean,

Can you tell me if it is ok to take *HerBalance™ Cream with Pregnenolone and Pregnenolone capsules (30 mg)* at the same time and if so what dosage?

I have chronic skin itching problems and have found these products have helped the problem although it hasn't entirely gone away. The progesterone has totally changed my life! I am no longer a depressed housewife, just itchy.

Your input into this would be greatly appreciated.

Kind regards,  
Mrs. W.

Dear Mrs. W.,

Yes, you can combine the *HerBalance Cream with Pregnenolone* and *Pregnenolone capsules*. Because the dosage requirement is different for different people, we offer 10, 30, and 100 mg *Pregnenolone capsules*. You can vary the combination to adjust the dose that works best for you. For the itchy skin, you might also try *Lithium Orotate* 1-2 capsules twice per day. *Lithium Orotate* is a great nerve stabilizer, and may help alleviate the itching.

Ward Dean, M.D.

## Atrial Fibrillation

Dear Dr. Dean,

**I occasionally get atrial fibrillation. What supplement would help my condition? I have been taking Pressure-Fx® and I feel it helps. It has been over two months since my last attack. Will Cardio Rhythm also help? I think CoQ10 will be harmful to my condition.**

Mr. D.

Mr. D.,

I agree with your idea about *Cardio Rhythm*. In addition, *DHEA* and *magnesium* have both been shown to be helpful for atrial fibrillation.

I disagree, however, with your concern about *CoQ10*. *Coenzyme Q10* is an essential mitochondrial coenzyme that is extremely important for heart health, and may be beneficial for you.

For atrial fibrillation, I also usually prescribe two medications, which you might discuss with your physician: *Dilantin*, 100-300 mg per day, and a beta blocker (such as *Inderal*®) to maintain a heart rate in the 65-75 beats per minute range.

Ward Dean, M.D.

## Autism

Dear Dr. Dean,

**My 15-year-old son is autistic, weighs 170 lbs, and has extreme behaviors and obsessions that cause him to talk to himself or repeat the same nonsense phrases 100 times daily to the point he cannot have a conversation at all. We have started 5-HTP as no drugs work for him. Based upon weight, how much 5-HTP can I give him daily and should I break it up—morning, mid-afternoon, evening—or give it to him all at once? Right now I give him 100-200 mg in the morning and the effects last until about 2 p.m.**

Thanks,  
Ms. H.

Dear Ms. H.,

In weight loss studies using *5-HTP*, doses up to 900 mg per day were administered. The most common dose-limiting side effect was gastrointestinal symptoms (diarrhea, upset stomach). The next most common side effect was sleepiness. At the doses you are currently using, you are well within the dosage range that is known to be safe.

I would try repeating the dose after lunch, supper, and perhaps again at bedtime. (Several hours after the meals, so as to be taken on an empty stomach).

In addition, I suggest 3-5 grams of *Trimethylglycine (TMG)*—also known as *Anhydrous Betaine*. *TMG* is a pleasant-tasting powder, and can be mixed in almost any beverage.

Also, consider *Lithium Orotate*, 1-3 caps twice per day. This may help with his obsessive-compulsive behavior.

Ward Dean, M.D.

## High Blood Sugar

Dear Dr. Dean,

**The normal blood sugar volume is around 100, but my dad has a level of 175 – 200. Can you please recommend what he should take to lower the volume?**

Thank You,  
Mr. L.

Dear Mr. L.,

I recommend your father start with *Optimum D*, a multi-nutrient formula designed to stabilize blood sugar. If that does not bring his blood sugar into a desirable range, add *GluControl*™, increasing the dose progressively until his blood sugar is in the normal range.

Ward Dean, M.D.

## Pericarditis, Thyroid Cancer

Dear Dr. Dean,

**I've had 3 bouts of pericarditis in the past 2 months. I'm told it may be viral or bacterial but no other cause. I have to take prednisone for a few days and that masks the pain but as yet there has been no cure. Do you have a suggestion?**

**I also have been diagnosed with thyroid cancer, papillary type. I have a history of tumors in various forms from head to toe both malignant and non-malignant. Any help will be appreciated.**

The Queen of Tumors,  
Mrs. W.

Mrs. W.,

As you know, pericarditis is inflammation of the pericardium, the sac enclosing the heart. Your thyroid cancer may be the cause of your pericarditis (or one of the other

tumors may be the cause).

First, I recommend the powerful anti-inflammatory multi-enzyme combination, *UniZyme*™, in high doses. Also, *Turmeric Extract*, 3 grams per day.

Finally, I recommend taking an *Iodine Sufficiency Test*, as well as *Iodoral*®, one per day. Please read the articles on our website about iodine/Iodoral.

Hope these suggestions help.

Ward Dean, M.D.

## Chicken Pox

Dear Dr. Dean,

**Are there any natural substances that can be used for chicken pox?**

Ms. S.

Dear Ms. S.,

Two suggestions are to use Oral/Topical *Mild Silver Protein*, applied topically to the lesions.

Another suggestion is to use *BHT* dissolved in *Coconut Oil*, applied topically, or *BHT* orally, in a dose of 500 mg per day (for adults). I don't recommend it for use in infants and children, as I have no experience in such use.

Immune system support would also be important. *Beta glucan* or *EpiCor*™ are two suggestions in this area, and are both safe for children.

Ward Dean, M.D.

## Root Canals

Dear Dr. Dean,

**What do I take to get rid of inflammation from root canals?**

Ms. L.

Dear Ms. L.,

If it's an old root canal, it is likely that you are developing an abscess.

The short-term response is to use a powerful antibiotic like *Clindamycin*. Unfortunately, there are probably some resistant bacteria that have "cooked" for quite some time, and the optimum solution may require that the tooth be extracted.

To improve overall dental health and to prevent the formation of future cavities, you may want to consider using xylitol (*Unique Sweet*®) gum and mints.

Ward Dean, M.D.

# Bone and Joint Health: The Second Component to Healthy Aging

by Chris D. Meletis, ND

In the January newsletter article, *Five Critical Components to Healthy Aging*, I touched upon the five most critical ways individuals can stay healthy throughout their lives. Last month, I began a five-part series to address each of these components in more detail beginning with the first component, cardiovascular health. This month, I will delve deeper into the second component of healthy aging: bone and joint health.

In the initial installment of *Five Components to Healthy Aging*, I wrote about the importance of maintaining healthy joints. In this follow-up article, I will explore the importance of bone health in both men and women since osteoporosis is one of the leading causes of disability in the elderly.

## Osteoporosis in Men

Before I address the factors that influence bone health in women, I would like to touch upon an often-overlooked fact: osteoporosis is a concern that affects both genders. Although osteoporosis in women has received substantial attention, its impact in men is also significant and noteworthy. In particular, men who are treated for prostate cancer with androgen deprivation therapy (ADT) may be at an especially high risk for osteoporosis.<sup>1-2</sup> Males with diabetes also have an increased osteoporosis risk.<sup>3</sup> Furthermore, millions of men suffer from andropause, which also contributes to osteoporosis (see my article on Andropause and Menopause in this edition of *Vitamin Research News*).

The good news is that the approaches used to strengthen bones in women may be equally useful in men.<sup>4</sup>

## Factors Affecting Bone Health

Our ability to maintain proper bone density is dependent upon a state of balance. Under normal conditions, an increase or decrease in bone resorption is coupled to a compensatory increase or decrease in bone formation. This creates a homeostasis between the bone-destroying cells known

as osteoclasts and the bone-building osteoblast cells. This balance protects against net bone loss.

The dramatic drop in estrogen, progesterone and androgens that occurs after menopause may be in part responsible for disrupting this bone-building homeostasis. Estrogen replacement has been the mainstay for osteoporosis prevention and treatment in this estrogen-deficient population. However, long-term compliance with estrogen therapy generally is poor, and there are numerous concerns regarding its safety.<sup>5</sup> Due to these concerns, bioidentical hormone replacement, which avoids some of the potential pitfalls of synthetic prescriptions, has become a clinically popular way to restore hormone balance. Dr. John Lee wrote extensively on the importance of using natural progesterone cream to enhance bone strength, an approach that can be used in both women and men.

The foods we eat also play an instrumental role in determining whether or not our bodies' bone-building mechanisms are knocked out of homeostasis. For example, calcium is known to affect one of the most important bone metabolism regulators, parathyroid hormone (PTH). Phosphorus also is an essential mineral for bone health. However, to protect against osteoporosis, the human body must maintain a balance between calcium and phosphorus. Excess phosphorus intake is common in people consuming the typical Western diet. Excessively high amounts of phosphorus are found in soft drinks and processed foods and meats. Too high a phosphorus intake is known to increase PTH secretion and lower calcium absorption, which could trigger bone destruction. When calcium intake is low, phosphorus also decreases bone formation markers and increases bone resorption markers.<sup>6</sup>

Caffeine intake can have an equally damaging effect on bones. Researchers

recently reported that women with caffeine intakes greater than 300 mg per day had higher bone loss than women consuming less caffeine. The scientists determined that caffeine may exert these damaging effects through its ability to influence the way vitamin D is metabolized by the body.<sup>7</sup> Coffee also can raise homocysteine levels, which further contributes to osteoporosis risk.<sup>8-9</sup> This indicates that vitamins B12 and B6 and folic acid, which lower homocysteine levels, may provide further bone-building support.

Other dietary factors that play a role in bone density are the widespread deficiency of nutrients important to bone health, such as vitamin D3 and vitamin K. Studies have shown that vitamin K intake from a normal diet is not enough to counteract the effects of a protein called osteocalcin that is involved in bone destruction. Supplementation with vitamin K reduces osteocalcin activity.<sup>10</sup>

Vitamin K has been especially effective at improving bone health when combined with vitamin D. Vitamin K enhances the function of bone-building cells known as osteoblasts and inhibits the function of bone-destroying cells known as osteoclasts. The evidence has steadily accumulated that Vitamin D3 supplementation, through its ability to enhance calcium availability, prevents bone loss in elderly women.<sup>11-12</sup> The anti-osteoporosis evidence in support of vitamin D3 is so extensive that the FDA is now allowing claims that this vitamin is important for bone health.

When vitamin K is combined with vitamin D, there appears to be an even greater effect. Vitamin K2 improved bone mass in patients with high vitamin D3 serum levels more than in patients with low vitamin D3 serum levels.<sup>13</sup> Other researchers reported that vitamin K2 enhanced mineralization caused by the bone-building osteoblast cells, but these effects differed in the presence or absence of vitamin D3 levels.<sup>14</sup>

One group of researchers found that

vitamin D3, when added to vitamin K2, promotes bone coupling and restores balance between osteocalcin and osteoblast faster than in untreated subjects or subjects taking only vitamin K2 or only vitamin D3.<sup>15</sup>

According to the researchers, “Vitamin K2, especially when combined with vitamin D3, can partially prevent bone loss caused by estrogen deficiency.”

### Equally Important Nutrients

Vitamin K and Vitamin D3 can be particularly effective when adding two other substances into the bone-building mix: ipriflavone and strontium.

Ipriflavone, a synthetic isoflavone, has proved supportive in bone health in estrogen deficient women. Italian researchers assessed the effects of ipriflavone administration in the prevention of the rapid bone loss that follows ovariectomy in women. Ten to 30 days after an ovariectomy, 16 patients consumed calcium supplements alone and another 16 patients received ipriflavone 600 mg per day plus calcium for 12 months. In calcium-treated subjects bone loss markers increased and radial bone density significantly decreased 6 months after surgery. However, in the group taking ipriflavone and calcium, the patterns of biochemical markers indicated that ipriflavone can restrain the bone destroying processes. In addition, com-

pared to the calcium-only group, where bone density decreased, radial bone density in the ipriflavone-plus-calcium group showed no significant modification.<sup>16</sup>

According to the researchers, “These results demonstrate that ipriflavone administration prevents the rapid bone loss that follows ovariectomy. Thus, ipriflavone can represent an attractive alternative for the prevention of osteoporosis in postmenopausal women who present contraindications to the estrogen replacement therapy.”

Strontium is another natural agent known for improving bone health. Strontium ranelate is the most studied form of this mineral. It is unique in its mode of action as it both decreases bone resorption and increases bone formation. Two clinical studies have demonstrated over three years that strontium ranelate can reduce vertebral and non-vertebral fractures including those of the hip. These same studies showed that strontium has an excellent safety profile. The only reported side effect in a small number of patients was they developed diarrhea when they consumed more than 2 grams per day. Furthermore, according to a January 2007 report in the medical literature, an analysis of a sub-group of patients aged 80 years and over demonstrated that, currently, strontium ranelate is the only anti-osteoporotic agent to reduce

vertebral and non-vertebral fractures in this age group.<sup>17</sup>

A study published in 2002 included 353 osteoporotic women with at least one previous vertebral fracture and low scores of lumbar bone density. Patients received placebo or strontium ranelate in doses of 170, 340 or 680 mg per day for two years. The results indicated that in the strontium group lumbar bone mineral density increased in a dose-dependent manner (Fig. 1). Also, there was a significant reduction in the number of patients with new vertebral fractures in the second year in the group receiving the 680 mg per day dose. In this same group, a significant positive change in markers of bone metabolism occurred. The authors concluded that strontium ranelate therapy increased vertebral bone mineral density and reduced vertebral fracture incidence.<sup>18</sup>

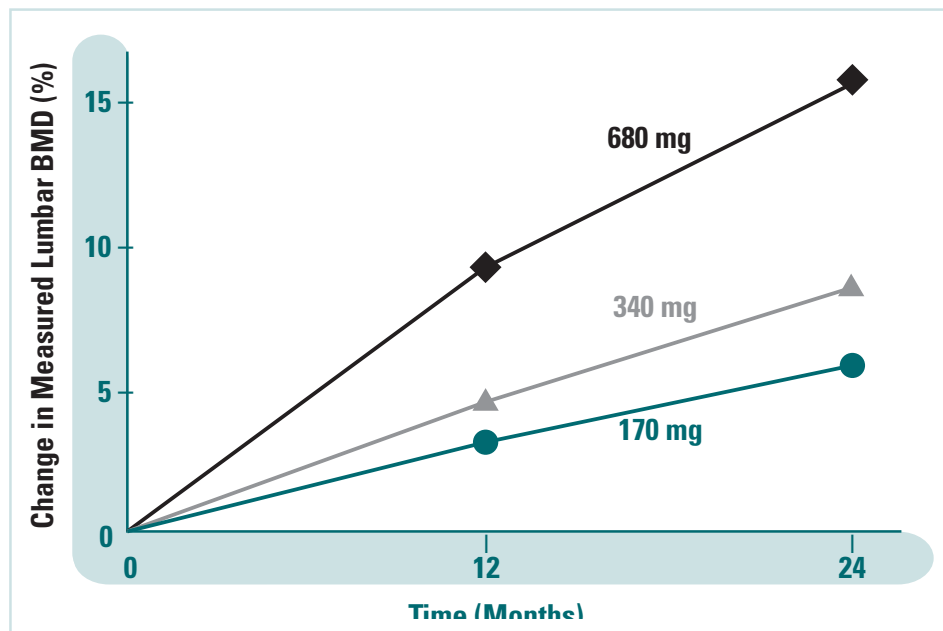
Although more recent studies use strontium ranelate, earlier studies showing similar results used other strontium salts, including strontium carbonate, strontium lactate, and strontium gluconate. Therefore, it appears that the active ingredient is strontium.

### Conclusion

The high prevalence of osteoporosis and related morbidity and mortality herald an enormous public health burden for the coming decades. Supplementing the diet with vitamin D3, vitamin K, ipriflavone and strontium—along with a good multimineral formula containing bone-building minerals such as boron—can ensure that our structural support systems stay healthy and strong.

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**Figure 1.** Increase in lumbar bone mineral density (as measured by dual energy X-ray absorptiometry—DXA) after two years treatment with strontium in doses of 170 mg per day, 340 mg per day, and 680 mg per day (Meunier, et al, 2002).

*Continued on page 14*

# Low Stomach Acid: Its Surprising Role in Gastric Health

by Nieske Zabriskie, ND

**H**ydrochloric acid (HCL) is an important part of healthy digestion. It is a strong acid produced by the parietal cells in the stomach generating a gastric pH of 2-3. Activation of digestive enzymes and absorption of nutrients relies on an acidic pH in the stomach. Pepsin, an enzyme required to break down protein for digestion, is activated by HCL, functions at a pH of 2-3 and is inactive in an environment over a pH of 5. HCL also is important to protect the stomach and intestines from pathogens and bacterial overgrowth such as *Escherichia coli* (*E. coli*) and *Helicobacter pylori* (*H. pylori*).<sup>1</sup> Low levels of HCL, known as hypochlorhydria, decrease absorption of nutrients and increase gastric inflammation, and are a risk factor for several diseases. Additionally, HCL decreases with age. In fact, a small study showed that 80 percent of individuals with a mean age of 84 were hypochlorhydric.<sup>2</sup>

## **Helicobacter pylori (H. pylori)**

*H. pylori* is a gram-negative bacteria commonly found in the stomach of individuals with gastritis and ulcers. Research has shown that more than 50 percent of the population worldwide is infected with *H. pylori*. Also, the prevalence of *H. pylori* increases with age. These bacteria colonize the mucosal lining of the stomach and cause several diseases including atrophic gastritis, dyspepsia, gastric and duodenal ulcers, iron-deficiency anemia, gastric cancer, and B-cell lymphoma of mucosa-associated lymphoid tissue (MALT). Evidence shows that in individuals infected with *H. pylori*, 15-25 percent have duodenal ulcers, 13 percent have gastric ulcers, and 1 percent develop gastric carcinoma.<sup>3</sup> It is believed that the progression from atrophic gastritis to metaplasia, dysplasia, and eventually to gastric cancer is caused by a decrease in HCL and protective mucins. *H. pylori* infection can cause hypochlorhydria depending on the location of infection in the stomach.

Gastric cancer is the second most common cause of death from malignancy

in the world. Infection with *H. pylori* increases the risk of gastric cancer six-fold. Achlorhydria, or the complete lack of HCL, increases the risk of stomach cancer by 4.7 fold.<sup>4</sup> Hypochlorhydria, whether it is caused by pharmaceuticals or disease processes, allows for bacterial overgrowth in the stomach. These pathogenic bacteria in the stomach can produce nitrite and nitroso-compounds. These compounds are carcinogens and evidence indicates they are inhibited by vitamin C in the stomach. Research has shown that individuals with atrophic gastritis and gastric cancer have increased pH and nitrite levels as well as decreased levels of vitamin C. Additionally, individuals with gastric cancer had higher levels of nitrite and lower levels of vitamin C compared to individuals with atrophic gastritis at the same pH.<sup>5</sup>

A large study found that in individuals with dyspepsia (indigestion), over 67 percent were infected with *H. pylori*. This bacterium was significantly more frequent in individuals with peptic ulcer disease than with non-ulcer dyspepsia. Additionally, this study demonstrated that in individuals with gastritis, 70 percent have *H. pylori*, in individuals with duodenal ulcers, 86 percent have *H. pylori*, and in individuals with gastric ulcers, over 71 percent have *H. pylori* infection.<sup>6</sup> With chronic gastritis, the parietal cells stop functioning correctly. In addition to secreting HCL, these cells also secrete intrinsic factor. Intrinsic factor is a protein required for the absorption of vitamin B12. Thus, low or no stomach acid may result in low vitamin B12 levels and pernicious anemia as well.

## **H. Pylori and Low Stomach Acid**

Conventional treatment for *H. pylori* infection is a triple therapy including proton-pump inhibitors combined with two antibiotics. However, treatment rarely returns HCL levels to normal. In fact, a study showed that after 5 years of eradication of *H. pylori*, the majority of patients did not have optimal HCL secretion.<sup>7</sup> Adequate nutritional status, particularly increased

consumption of fruits and vegetables and vitamin C, appears to be protective against *H. pylori* infection.<sup>8</sup>

## **Increasing Stomach Acid**

Evidence in a clinical setting suggests that improvement of HCL levels and decreased gastric pH may improve gastrointestinal symptoms and decrease disease risk. Alternative medical providers often prescribe supplemental betaine HCL to treat hypochlorhydria and related conditions. Combining HCL with pepsin may improve digestion of protein as well.

Peppermint is another agent used for numerous digestive complaints such as dyspepsia. It provides antispasmodic activity on the smooth muscle of the intestines and relaxes the lower esophageal sphincter. Research indicates that peppermint exhibits antibacterial activity against *Salmonella enteritidis*, *Escherichia coli*, *Staphylococcus aureus*, and *H. pylori*.<sup>9</sup> Gentian root, historically used for digestive complaints such as gastritis, complements peppermint's actions. A recent study showed that both gentian root and peppermint inhibit the growth of *H. pylori* in vitro.<sup>10</sup>

Low stomach acid secretion is a risk factor for numerous diseases, including infection by *H. pylori*. Eradication of this bacterium is imperative to optimize digestion. The fact that HCL decreases with age and due to the wide use of acid-blocking pharmaceuticals, natural agents may be useful to prevent the progression of conditions such as bacterial overgrowth, dyspepsia, and gastric cancer.

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# Acetylcholine

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(lipofuscin)—the brownish pigment that causes “liver spots” (lentigo) on the backs of the hands of many people over 50 years of age.

DMAE not only can prevent the formation of lipofuscin, but it also actually flushes it from the body.<sup>23</sup> Many people gauge the rate of lipofuscin removal from their hearts and brains by watching their “liver spots” disappear with long-term supplementation of DMAE. It usually takes about six months for significant changes to take place—with many spots resolving completely.

## Conclusion

A recent study reports that approximately 24 million people suffer from dementia worldwide. If the mortality rate does not change and no curative or preventive treatment is developed, this number is expected to double every 20 years.<sup>24</sup>

With this threat hanging over our heads, DMAE and galantamine deserve high rankings on the list of cognitive-enhancing supplements. Each of these natural agents has a long track record of safety and efficacy, and ongoing research continues to add to the already impressive list of potential benefits.

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# NUTRITION REVIEW

## Chromium Picolinate and Biotin Help Control Healthy Blood Sugar Levels

Researchers from Yale University have found that supplementation with chromium picolinate plus biotin can improve glycemic control in type 2 diabetic patients who are not responding to oral antihyperglycemic agents.

Preclinical studies have shown that the combination of chromium picolinate and biotin significantly enhances glucose uptake in skeletal muscle cells and enhances glucose disposal. The authors of the current double-blind, placebo-controlled trial decided to take these previous investigations one step farther by determining how these two nutrients affect blood sugar control in humans.

Forty-three obese or overweight subjects with impaired glycemic control despite

treatments with oral antihyperglycemic agents were randomized to receive 600 micrograms of chromium picolinate and 2 mg of biotin per day. Researchers measured glycemic control and blood lipids at baseline and after 4 weeks.

At the study's end, there was a significant reduction in glucose during the 2-hour oral glucose tolerance test in subjects taking the chromium and biotin compared with the placebo group. Glucose tolerance improved by 15 percent in subjects taking the two nutrients. The subjects taking the chromium and biotin also experienced significantly greater reductions in triglycerides and triglycerides to high-density lipoprotein cholesterol ratio. Triglyceride levels decreased by 9.25 milligrams per deciliter in the chromium picolinate/biotin group, and increased by 59.75 mg per dL in the placebo group.

Fructosamine levels, a marker of diabetic control, were also found to improve in the subjects consuming chromium and biotin, with a measured reduction of 1.3 millimoles per liter of serum. Levels increased in the placebo group by 0.7 millimoles per liter of serum.

No significant adverse events were attributed to chromium picolinate and biotin supplementation.

According to the researchers, “Chromium picolinate/biotin supplementation may represent an effective adjunctive nutritional therapy to people with poorly controlled diabetes with the potential for improving lipid metabolism.”

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## NUTRITION REVIEW

### Folic Acid May Help Preserve Hearing As We Age

Folic acid may slow age-related hearing loss in older men and women, a new study indicates.

Past studies have linked low folate to poor hearing. Consequently, researchers organized a double-blind, randomized, placebo-controlled trial that included 728 men and women aged 50 to 70. At the study's start, subjects had plasma total homocysteine concentrations on the upper end of the normal range, and no middle ear dysfunction, unilateral hearing loss, or pathologic ear conditions unrelated to aging. The subjects were randomly divided to consume either 800 micrograms per day of folic acid supplements or a placebo for three years.

The researchers report that, at the study's start, the average threshold for hearing in the low-frequency range was 11.7 decibels, and 34.2 decibels in the high-frequency range. At the study's end the thresholds had increased for both folic acid and placebo groups, meaning a louder noise was

required before the participants could hear the sound. However, in the low-frequency range, subjects who consumed the folic acid experienced a reduced increase in this threshold compared to the placebo group, so that they did not require as much of an increase in a sound before they could hear it. No significant difference in threshold decline in the higher frequency threshold was observed. The researchers theorize that hearing loss may be related to homocysteine levels and folic acid's effect may be due to its homocysteine-lowering ability.

In an accompanying editorial, an University of California, Davis researcher commented that if such a benefit could be applied to the general population, folic acid supplementation for a longer period could result in a five-decibel decrease in age-related hearing loss over 20 years, leading to a significant reduction in the need for hearing aids.

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Durga J, Verhoeve P, Anteunis LJ, Schouten E, Kok FJ. Effects of folic acid supplementation on hearing in older adults: a randomized, controlled trial. *Ann Intern Med.* 2007 Jan 2;146(1):1-9.

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Product	Code
5-HTP .....	CP5767
AdaptaPhase® I .....	CP1910
Allay™ .....	CP1660
Anhydrous Betaine.....	CP1412
Beta-Glucan .....	CP5044
BHT.....	CP8010
Cardio Rhythm.....	CP1950
Coconut Oil .....	CP3216
CoQ10-H <sub>2</sub> ™ .....	CP6300
DHEA.....	CP6371
EpiCor™ .....	CP1490
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## Ginkgo May Enhance Cognitive Health

Ginkgo biloba suppressed pathological behaviors associated with the destructive protein known as amyloid-beta, and prevented its toxicity in an in vivo model of Alzheimer's disease.

Amyloid-beta toxicity has been postulated to initiate the synaptic loss and subsequent neuronal degeneration seen in Alzheimer's disease (AD). The researchers of the current study had previously demonstrated that a standardized ginkgo biloba extract inhibits amyloid-beta-induced cell death in neuroblastoma cells.

In this study, researchers used ginkgo and its single constituents to study amyloid-beta and amyloid-beta-induced pathological behaviors in *Caenorhabditis elegans*, a worm that served as a model organism. The results indicated that ginkgo and one of its components, ginkgolide A, alleviates amyloid-beta-induced pathological behaviors, including paralysis. In addition, the ginkgo reduced the process known as chemotaxis, the movement of additional white blood cells to an area of inflammation in response to chemical mediators. Furthermore, the ginkgo inhibited amyloid-beta deposits.

The researchers also tested ascorbic acid (vitamin C) and found that even though the ascorbic acid reduced intracellular levels of hydrogen peroxide (a harmful pro-oxidant) to the same extent as ginkgo, it was not nearly as effective as ginkgo in suppressing paralysis. Consequently, they concluded that oxidative stress reduction is not the mechanism by which ginkgo and ginkgolide A suppress amyloid-beta paralysis.

The study authors concluded that their findings suggest that ginkgo suppresses amyloid-beta-related pathological behaviors and that ginkgo and ginkgolide A have "therapeutic potential for prevention and treatment of Alzheimer's."

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Wu Y, Wu Z, Butko P, Christen Y, Lambert MP, Klein WL, Link CD, Luo Y. Amyloid- $\beta$ -Induced Pathological Behaviors Are Suppressed by Ginkgo biloba Extract EGb 761 and Ginkgolides in Transgenic *Caenorhabditis elegans*. *The Journal of Neuroscience*. December 13, 2006; 26(50):13102-13113. [E pub Ahead of Print].

## Prebiotics Important for Artery Health

The prebiotics known as oligofructose (also called Fructooligosaccharide) and inulin significantly inhibited plaque build up in the arteries of rodents, a new study has found.

Scientists studied the effects of inulin and oligofructose on atherosclerotic plaque formation in male mice deficient in apolipoprotein-E, which is required for the normal breakdown of triglyceride-rich lipoprotein constituents. The apolipoprotein-E deficiency increased the animals' risk of heart disease.

Thirty-two mice were randomly divided into five groups. The control group received a semi-purified sucrose-based diet for 16 weeks. In the other groups, the sucrose was replaced in part by either inulin fructans, long-chain inulin, oligofructose, or an oligofructose-enriched inulin. The researchers then assessed the presence of atherosclerotic plaques.

The mice fed long-chain inulin or an oligofructose-enriched inulin had approximately 35 percent and 25 percent reduced atherosclerotic lesion area compared with the control group. Feeding long-chain inulin significantly reduced plasma cholesterol concentrations, and the inulin-type fructans reduced triglyceride concentrations compared with the control group. Both the long-chain inulin and the oligofructose-enriched inulin significantly lowered liver cholesterol concentrations compared with the control diet. Liver triglyceride concentrations also were significantly lower in all three groups fed the fructan-supplemented diets compared to the control group.

According to the study authors, "The results of the present study suggest that inhibition of atherosclerotic plaque formation is more potent in the presence of long-chain inulin, either alone or in combination with oligofructose (an oligofructose-enriched inulin), and that this probably is related to changes in lipid metabolism."

### Reference:

Rault-Nania MH, Gueux E, Demougeot C, Demigne C, Rock E, Mazur A. Inulin attenuates atherosclerosis in apolipoprotein E-deficient mice. *Br J Nutr*. 2006 Nov;96(5):840-4.

Anyone who wants to consume these two prebiotics can supplement with *Culturelle*<sup>™</sup>, which contains inulin, and *BioPro*<sup>™</sup>, which contains oligofructose (Fructooligosaccharide).

## Cranberries May Have Anti-Tumor Properties

A new review of the medical literature indicates that cranberries inhibit the proliferation of a number of cancers.

The researchers reviewed the existing research on cranberries and the key phytochemicals that are likely contributors to its chemoprevention properties. After examining the in vitro evidence on how cranberries affected a variety of tumor models, they concluded that polyphenolic extracts from cranberries inhibit the growth and proliferation of breast, colon, prostate, lung, and other tumors. Flavonols, proanthocyanidin oligomers, and triterpenoids isolated from the fruit have demonstrated equally promising effects, the reviewers noted.

According to the University of Massachusetts researchers, the unique combination of phytochemicals found in cranberry fruit may produce synergistic health benefits.

After studying the literature, they also found that the evidence suggested possible mechanisms of action of cranberry's phytochemicals. These mechanisms of action included induction of apoptosis (cell death) in tumor cells, decreased expression of matrix metalloproteinases associated with prostate tumor metastasis, and anti-inflammatory activities including inhibition of cyclooxygenases.

The reviewers concluded, "These findings suggest a potential role for cranberry as a dietary chemopreventive and provide direction for future research."

### Reference:

Neto CC. International Research Conference on Food, Nutrition, and Cancer. Cranberry and Its Phytochemicals: A Review of In Vitro Anticancer Studies. *J Nutr*. January 2007;137:186S-193S.

# Vitamin Research News

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