Introducing

A UNIFYING THEORY OF AGING

Longevinex® is more than resveratrol

Supplement Facts

Serving Size: 1 capsule
Servings per container: 30

Amount Per Serving		% Daily Value
Total Calories	3.78	
Calories from Fat	3.78	
Total Fat (grams)	0.42 g	0.65%
Vitamin E as mixed tocopherols 90%	5 mg	~15%
Proprietary Longevinex® blend of French red wine extract and Giant knotweed (*Polygonum cuspidatum*) leaf extract providing 100 mg of trans resveratrol per capsule	215 mg	*
Quercetin Dihydrate	25 mg	*
Rice Bran Extract (IP6)	75 mg	*
Rice Bran Oil	380 mg	*
Sunflower Lecithin	55 mg	*

% Daily Values are based on 2,000 calorie diet.
* Daily value not established

Other ingredients: Gelatin, vegetable stearate (flow agent), titanium dioxide (inert)

Newly Formulated Longevinex® now features

more trans resveratrol and IP6 phytate in a base of rice bran oil

Ingredients in Longevinex® address the many theories of aging.

(Print out of this report is about 59 pages)

Topic: Theories of aging addressed by Longevinex®.

While resveratrol has recently gained widespread public and scientific attention for it age prolonging qualities, Longevinex® is a unique multi-ingredient dietary supplement that is more than just resveratrol.

The ingredients in Longevinex® are designed to address five major theories of aging: the free radical/antioxidant theory, the hormonal theory (estrogen/testosterone), the mitochondrial (cell energy) theory, the cell cleansing or autophagy theory, and the metabolic, calorie restriction/Sirtuin gene activation theory.

There is another theory of aging, also addressed by the ingredients in Longevinex®, which may supercede and better explain other theories of aging. It is proposed here.

Introduction: Why slow aging?

There are many theories as to why humans age prematurely and what can be done to slow the rate of aging. Slowing the onset of aging is critically important since most chronic disease is age related. A recent goal was announced by a consortium of researchers involved in the study of human aging. The objective is to delay the onset of aging by seven years, thus pushing off the onset of age-related disease and adding more healthy years of life, which would save Medicare from its predicted financial demise.[1]

The idea of living more youthful years is now at hand since the mapping of the human genome and the knowledge that individual genes control aging. Increasing the healthspan and lifespan is within reach, as these strategies improve both the quality and quantity of life.[2]

Despite the fact more Americans are overweight and have diabetes (now coined the diabesity epidemic), more Americans are living longer than ever thought possible. About one in four 65-year old adults will live to age 92 or beyond.[3] That is a staggering figure.

In recent times it has become apparent that humans can immediately begin to put into practice certain age-delaying tactics, the most prominent and accepted anti-aging regimen being calorie restriction. While food deprivation is not likely to be widely practiced, its molecular mimic, resveratrol, is now being touted as a metabolic shortcut to avert the frailties and senility associated with advanced age. For example, a recent experiment demonstrated that resveratrol-fed mice given a high-fat diet retained their motor skills (balanced and coordination) as well as mice on a lower-calorie diet.[4]

While resveratrol has broad biological action, it does not fully address all of the major biological pathways to control aging.

MAJOR THEORIES OF AGING
Antioxidant/free-radical theory
Hormonal theory
Mitochondrial mutation theory
Cell debris/cleansing theory (autophagy)
Calorie-restriction or resveratrol
mimic theory of aging

An alternate and unifying theory of aging

There is another theory of aging, proposed here, which has been overlooked – over-mineralization. The rate of over-mineralization in the human body parallels the rate of aging.

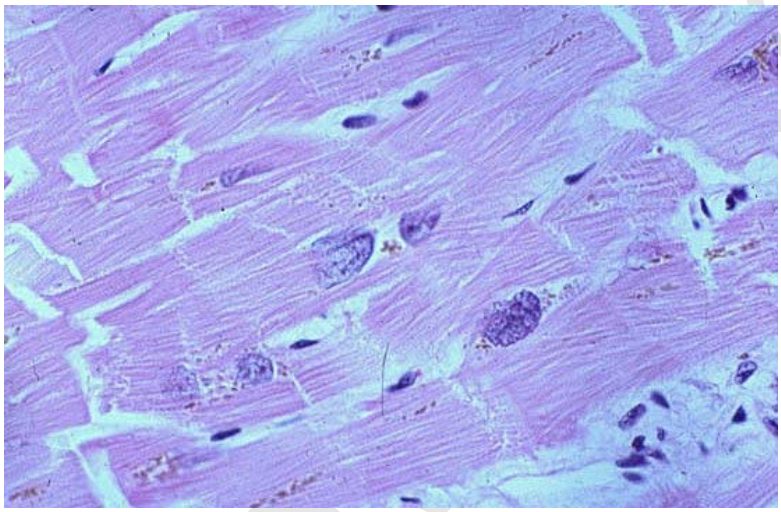
The gradual overload of minerals, particularly calcium and iron, which are the predominant minerals in bone and blood, explain a great deal of aging, and partially if not totally explain the free radical, the mitochondrial, the hormonal and the calorie-restriction theories of aging.

As an oversimplification, the human body rusts and calcifies (turns into a statue) over time.

Calorie restricted diets and vegetarian diets are known to prolong human life and both obviously limit the amount of calcium and iron consumed.

When does aging begin?

During the years of growth, birthdays occur, but aging really doesn't begin till full growth is achieved, usually around age 18. Birthdays occur, but aging changes in tissues don't accelerate till full growth is achieved.



Lipofuscin aging pigments, seen above, are generated by excessive iron and are increasingly found in tissues throughout the human body with advancing age.

For example, the amount of an aging pigment (called lipofuscin) within the cytoplasm of rabbit cells is miniscule, representing only 0.29% of the cytoplasm volume at 12 months of life, whereas it reaches 2% of cytoplasm volume at 79 months (7 times increase).[5]

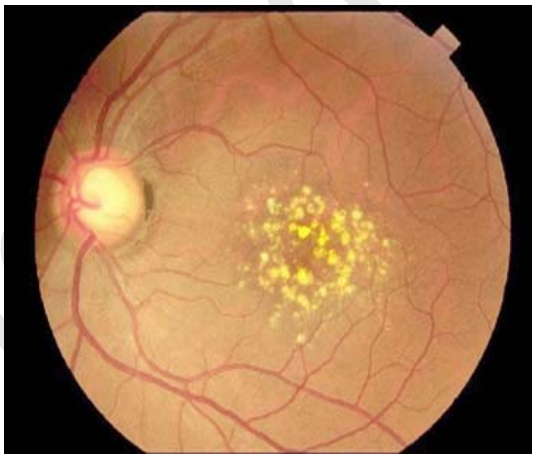
During growth years, all of the iron that is ingested is directed toward the production of new red blood cells (millions must be produced every second) and calcium is shuttled to develop bones. So it is very difficult to develop iron or calcium overload during youth. In fact,

this may explain why the first two decades of life are largely free of disease.

Even the symptoms of hereditary iron overload (hemochromatosis) do not emanate till age 12-18.[6]

Accumulation of cellular debris (lipofuscin) at the back of the human eye (retina) does not begin till age 19.[7]

Retinal lipofuscin deposits, induced by iron and calcification in retinal tissues, are generally not found until the 3rd decade of life, and more advanced cellular garbage deposits in the retina, called drusen, aren't normally observed during an eye examination till the 5th decade of life.[8]



Retinal drusen, seen early in child with premature aging syndrome.

Retinal drusen was reported in a young girl with a premature aging syndrome (Bloom syndrome). The girl was admitted to the hospital for failure to grow.[9]

Progeria is considered a disease of premature aging. It is characterized by calcification of arteries and heart valves. Generally, children with progeria are of short stature (~3 feet in height) and their demand for calcium for bone formation is reduced compared to healthy children.[10]

When full is growth achieved, the demand for iron and calcium diminishes and excesses can begin to accumulate.

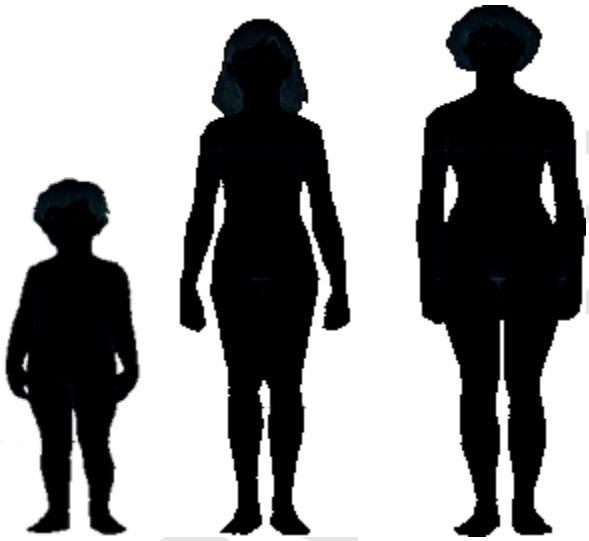
Gradual iron overload

Most well-nourished people in developed countries have 3-4 grams (3000-4000 milligrams) of iron in their bodies. Of this, about 2.5 grams (2500 milligrams) is contained in the red blood cell hemoglobin pigment that carries oxygen as blood circulates through arteries and veins. As red blood cells die, their iron is recycled to bone marrow to make new blood cells.

About 1 milligram of excess iron accumulates daily in males after full growth is achieved, which results in about 5000-8000 excess milligrams of stored iron in a male by age 40. A 45-year old male has as much iron in his blood circulation as a 70-year old female. At age 45 a male has four times as much iron stored in his body as females at this age, and has a heart attack rate four times that of women.[11]

A female however will dump excess iron via monthly menstruation (about 30 milligrams) and have half the iron

load of a male at age 40. Iron overload results in middle age males having twice the iron load as an equal-aged female and twice the rate of diabetes, cancer and heart disease. If females undergo early hysterectomy, then they will develop the same disease rates as males. In females iron overload begins much later, with menopause, and women live on average about 5-8 years longer than men.



FEMALES: High demand for calcium and iron during growth and reproductive years

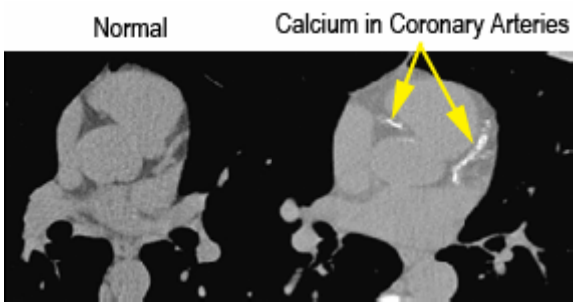
Proof of the theory of over-mineralization and aging

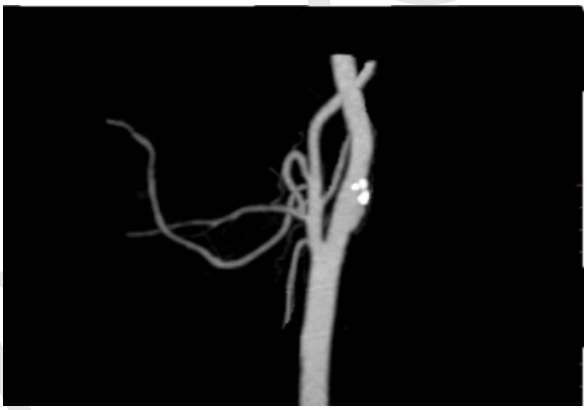
Calcification

Calcium is the most abundant mineral in the body. Of the two to three pounds of calcium contained in the human body, 99% is located in the bones and teeth.

There are inborn ways to limit calcification in nature. For example, elk avoid over-calcification by periodically shedding its antlers. Female mammals avoid over-calcification by donating calcium to their offspring.

Later in life, as estrogen production wanes, calcium is released from women's bones and enters the blood circulation where it clogs and hardens arteries (arteriosclerosis), the gallbladder (gallstones), heart valves (mitral valve), and kidneys (kidney stones). The main source of the calcium deposits is the bones. Over time, there is loss of calcium from bones, which become brittle and fracture (osteoporosis).[12]





Artery with small amount of calcified plaque

Many studies confirm the problem of over-calcification in humans. In a study of 582 aortas from humans (the aorta is the first blood vessel outside of the heart), it was shown that only 4% of patients aged 20–30 years had significant aortic calcification, which increased to 98% in individuals above 50 years.[13]

It is suggested that the calcium content of arteries may increase 30 to 40 times in a lifespan.[14]

Calcification of the aorta (first blood vessel outside of the heart) is greater and progresses faster among women who experience calcium/bone loss with the onset of menopause.[15]

The Klotho gene is involved in longevity. Activation of the klotho gene extends the life of mice by 19-31%.[16] It is interesting to note that a defect in the expression (activation of proteins) of the Klotho gene in the mouse, which results in extensive calcification and loss of elasticity of the aorta, produces a syndrome that mimics human aging.[17] Furthermore, iron overload switches off the Klotho gene, while iron chelation re-activates the production of Klotho gene proteins.[18]

Calcification of the pineal gland

The body's clock or synchronizer is the pineal gland, located at the base of the brain. At night, when the eyes are closed, the pineal gland secretes a strong antioxidant hormone, melatonin, which also induces sleep. Melatonin has drawn great attention as an anti-aging hormone.[19] With calcification of the pineal gland comes reduced production of melatonin.[20] Calcification of melatonin-producing cells in the pineal gland is more prevalent in old versus young animals.[21]

Over a decade ago it was demonstrated that the replacement of the pineal gland of an old mouse with the pineal from a young, donor mouse, remarkably prolongs its life and,

conversely, the *"old"* pineal gland transplanted into a younger mouse will considerably shorten its life span.[22]

The pineal gland, located at the base of the brain, secretes melatonin during sleep. This hormone has strong reparative and antioxidant properties and also controls sleep. Melatonin levels decline gradually over the life-span and are related to sleep problems, very often associated with advancing age.[23]

The increasing degree of pineal calcification may result in a decrease in melatonin secretion by the pineal gland, which subsequently may lead to a disturbed sleep-wake cycle, with the principal symptom being daytime tiredness, often experienced among older adults.[24]

A theory was presented in 1990 that the pineal gland is a centralized clock that controls aging, and that the calcification process occurring within the pineal gland *"provides a highly accurate bio-inorganic timing mechanism."*[25]

Researchers indicate melatonin is a prime candidate for slowing the aging process. Melatonin is described as having profound *"gerontoprotective"* and antioxidant activities. Supplementation with melatonin *"may become a promising, safe, and effective intervention strategy to slow aging and the initiation and progression of age-related disorders."*[26]

In postmortem examination of 33 human subjects (age range 3 months to 65 years), calcium deposits in the pineal gland correlated with advancing age and calcium levels correlated with a decline in melatonin content.[27]

Even though oral melatonin supplementation has proven to help with sleep problems, low melatonin levels are not related to sleep disturbances, nor does it predict response to melatonin replacement therapy. Researchers theorize individual differences in body and glandular size confounds an accurate understanding of melatonin biology. In Germany a method was devised to measure the degree of pineal gland calcification using computed tomography. The size of the pineal gland and its uncalcified volume was estimated and was correlated with melatonin levels. Researchers concluded that the decline in melatonin secretion with advancing age *"can be sufficiently explained by an increase in pineal calcification."*[28]

Of great interest is the discovery, that while some calcification of the pineal gland occurs in the first six years of life, there is a steep rise in the incidence of pineal calcification during the second decade of life, which coincides with slower body growth rates.[29] A study shows that the frequency of pineal calcification is 3% in the first 12 months of life rising gradually to 7.1% in children at 10 years of age. From 10 years onwards, there is a marked increase of frequency of calcifications of the pineal gland up to 33% in the group of children of 18 years of age.[30]

The mouse experiment

Animal experiments provide evidence for the iron overload theory of aging.

A research experiment conducted at the University of Texas Health Science center in San Antonio, Texas, is telling. The level of oxidation in various organs of mice was measured at 6, 12, and 24 months of age. The more food these animals consumed, the greater the accumulation of iron in their tissues, and the greater the amount of oxidation (aging) in these tissues. The accumulation of iron in these animals did not appear till full growth had been achieved, or after 355 days. After that time, iron in the liver increased by 140 percent and in the kidneys by 44 percent. The greatest buildup of iron in these animals with advancing age was measured in the liver and brain. Dietary restriction markedly reduces oxidation and iron levels in tissues throughout the body.[31]

Fruit fly experiments

Fruit flies (*Drosophila melanogaster*), because of their short life span (a few weeks), are often utilized in research studies because they can be used to quickly evaluate anti-aging strategies. Two compelling experiments were conducted in fruit flies to determine the role of iron in aging.

In the first experiment, it was found that iron accumulates in fruit flies throughout life. The rate of

iron accumulation was found to be proportional to the rate of aging in this species and *"may be the initiator of senescence,"* said researchers.[32]

In the second experiment, the life span of male fruit flies was found to be proportional to the iron content in the diet. The same is true for mice and humans. Furthermore, the total body iron count in fruit flies correlates with the total calcium load. The inclusion of tea extracts in the diet of fruit flies was found to inhibit the ageing-related accumulation of iron and to prolong their life span by as much as 21.4%. Researchers concluded that iron accumulation is a significant factor contributing to senescence.[33]

Iron and disease

Iron plays a predominant role in virtually every disease. For example:

All age-related brain diseases (Huntington's, Alzheimer's, Parkinson's) are caused by the release of fee iron in brain tissues.

Insulin resistance and Type II diabetes are aided and abetted by iron. Fatty liver, a condition that affects 35% of Americans, results from excess iron being stored in the liver.[34]

Cancer cells utilize iron as their primary growth factor, as do bacteria, viruses and fungi.[35]

Ageing is associated with an increased sensitivity of heart tissues to hydrogen peroxide formation, which is reversed by iron removal (chelation).[36]

Old cells have 10-fold more iron content than young cells.[37] As cells age, they accumulate iron-generated cellular debris called lipofuscin (age pigment), which clogs the cell and impairs cellular functions. Iron chelators are proposed to retard or erase lipofuscin (lie-poh-fus-kin).[38]

Iron reduction

Menstrual loss of iron gives a longevity advantage to females. The relative risk for death is nearly doubled for females who experience menopause at ages younger than 40 years.[39]

Francesco Facchini is a leading researcher on the role of iron, aging and disease. His research reveals that restriction of iron from the diet slows the progression of diabetic-induced kidney disease better than protein restriction. Survival rates nearly double by restricting iron in diabetics with kidney problems.[40]

The provision of an iron-poor diet to adults with blood vessel disease (atherosclerosis), even though they had normal iron levels as measured by blood testing, results in significant reductions in blood pressure, triglycerides, total and LDL cholesterol, blood sugar and

blood-clotting factors. This positive effect is less beneficial in premenopausal females who already control iron via menstruation.[41]

There is a great deal of research on the role of insulin and aging.[42] Researchers at the Massachusetts General Hospital have discovered a gene used by worms to regulate how much it eats and how fat it becomes, as well as controls how long it lives, is a gene strikingly similar to the gene for the insulin receptor, the factor that permits insulin to enter cells.[43]

In research conducted at Brown University, when the signaling from insulin-like proteins is reduced it results in increased life span among worms, fruit flies and rodents. In virtually all species, the slowing down of insulin production, or blockage of its signals to cells, can slow aging.[44]

Insulin, required by cells to burn sugar, often cannot enter cells due to a problem called insulin resistance. The problem appears to be age related. The removal of iron by blood-letting to near deficiency levels normalizes liver enzymes and brings about a 40-55 percent improvement in insulin concentrations.[45]

In another study researchers compared the efficiency of insulin to dispose of glucose (sugar) among meat eaters. Meat provides a readily absorbable form of dietary iron. All of the subjects in the study were lean, healthy and had no insulin metabolism problems. When iron levels were

depleted among meat eaters there was a 40 percent improvement in their ability to dispose of glucose/sugar. Iron load is critically important in the control of insulin and sugars in the body.[46]

Evidence is accumulating that free-radical production is increased in patients with iron overload, which can result in DNA damage and malignancies. Although blood-letting is effective at removing excessive iron, chelation (removal) therapy is required in many patients with iron overload.[47]

Iron exerts influence over calcium

Surprisingly, iron exerts control over calcium in many ways. Low molecular weight iron, known as ferric lactate, is very effective at inducing calcification in soft tissues.[48] When low molecular weight iron is injected into animals, heart tissue shows a very high increase in calcium influx.[49]

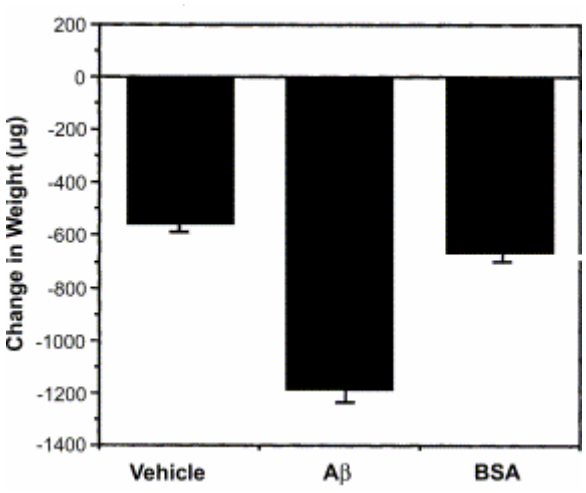
Iron also exerts control over calcium at the cellular level. The uncontrolled influx of calcium is the most common way of inducing cell death. Low-molecular weight iron complexes (ferric lactate) induce calcium deposition in the liver, resulting in cell death.[50]

An interesting experiment at the University of Utah appears to demonstrate the over-riding dominance that iron plays in calcium deposition in bones. As estrogen levels decline in menopausal women, calcium is lost from bones, resulting in a condition called osteoporosis. Female rats whose ovaries had been removed, and thus produced lower

amounts of estrogen (some is still produced in adrenal glands and fatty cells), which replicates the menopausal state of women, were given an iron chelator (remover) to prevent iron accumulation. As excess iron was chelated out of the body, there was a slowing in the loss of bone mass. Reduction of iron accumulation in post-menopausal females may avert osteoporosis.[51]

Iron, calcium and brain aging

Mark Mattson PhD, of the Sanders-Brown Research Center on Aging at the University of Kentucky, has conducted experiments to show how beta amyloid, the toxic molecule that accumulates in brain with advancing age, and is associated with Alzheimer's disease, adversely alters the regulation of iron and calcium in the brain. In one experiment Dr. Mattson incubated iron nails in water, albumin or beta amyloid. The amount of iron lost from the nails placed in beta amyloid was double that of nails placed in water or albumin. Water is known to rust nails, but beta amyloid hastened rusting more than water. This experiment was performed to demonstrate the destructive role of iron in brain aging.[52]



Decline in iron content of nails placed in water, beta amyloid (Aβ) or albumin (BSA).

Dr. Mattson also reports that beta amyloid destabilizes brain cells (neurons) so they can no longer regulated intra-cellular calcium levels. Beta amyloid compromises the ability of the neurons to reduce intracellular calcium levels to normal limits.[53]

Common health practices control iron

It is interesting that many popular health practices counter iron over-mineralization. Physical exercise, even a walking program, reduces iron stores.[54] Drinking tea with meals inhibits iron absorption from foods.[55] An aspirin tablet causes a slight amount of blood loss, which results in iron loss.[56] Calorie restriction or fasting obviously results in reduced iron intake. Calcium is widely believed to be a healthy dietary supplement, and it inhibits iron absorption.[57]

Copper

Other metallic metals also accumulate in the body with advancing age during the adult years. The human body holds about 72 milligrams of copper. Copper overload disease is called Wilson's disease. Iron overload is called hemochromatosis. Both maladies result in liver problems, systemic heart and blood vessel disease and shortened lifespan.[58]

Wilson's disease may serve as an interesting model of aging in regards to this essential mineral. The age of onset of copper overload (Wilson's disease) varies from age 12 to 40 years. Apparently during the growing years when copper is needed for growth, the disease does not emanate. But over time, copper accumulates, usually in the liver where it is stored, or the brain, where it may be released, causing symptoms that prompt a visit to the doctor. Buildup of copper in the liver increases mortality rates. If left untreated, most Wilson's disease patients would succumb at an early age to this disorder.[59]

Under normal conditions iron and copper are bound to transport proteins (ferritin and ceruloplasmin respectively) and do not cause *"rust"* or tissue damage in the body. But under certain conditions they can be set free to damage tissues, induce DNA mutations and raise cholesterol.[60]

The p53 tumor suppressor gene is frequently studied in models of cancer and aging. Investigators at the National

Cancer Institute have found that iron and copper cause mutations in this gene, rendering it useless in the fight against cancer.[61]

Copper is more of a toxin to brain cells than iron or zinc.[62] Copper and iron chelation (removal) are strategies to treat Alzheimer's disease.[63]

Brain aging and supplemental iron and copper

If rats are a reliable model of brain aging, supplemental metals in the diet such as iron or copper may accelerate brain aging, according to a report published by researchers at McGill University in Montreal.

Three groups of rats were compared in this study. Group 1 consumed rat chow at will. Group 2 consumed a 40% reduced-calorie diet that would provide less metallic minerals. Group 3 consumed a calorie-restricted diet with added minerals.

After 22 months, brain tissue from the three groups of rats was analyzed. Dietary restriction did NOT reduce the number of aging deposits in brain tissues compared to rats fed a normal diet, though reduced calories did reduce the number of aging brain deposits compared to the group that consumed restricted calories but received supplemental minerals.

The accumulation of aging deposits in the brain tissues of these animals was not accelerated during youth.

This is a key study to understanding aging because it underscores the importance of limited minerals rather than limited calories in the control of aging.

Scientists believe the *"curtailment of dietary trace metals" or "metal chelation (removal) therapy"* may have a beneficial effect on slowing the rate of brain aging.[64]

Experiments with monkeys ranging in age from 4 to 32 years show that as iron accumulates in the striatum and substantia nigra portions of the brain with advancing age, the balance and coordination (motor function) of these animals declines. The decline in motor function caused by iron exceeded the rate of decline caused simply by aging.[65]

Researchers at McGill University in Montreal report that oxidation, induced by deposition of iron in brain tissues, leads to mitochondrial insufficiency in brain cells which produces a degenerative central nervous system that is incongruent with and cannot be separated from brain aging. (The mitochondria are small organs within living cells that produce cellular energy.)[66]

When metallic mineral levels in biological fluids were evaluated in 60 subjects with Alzheimer's disease, the most significant result was a strong relationship between blood calcium and iron levels and the severity of mental impairment.[67]

The provision of iron and copper solely from the diet, rather than dietary supplements in full-grown males and

postmenopausal females, may be wise. While foods fortified with high amounts of iron and copper may be beneficial for growing children, they may not be appropriate for adults.

Iron overrides the estrogen theory of aging

The hormonal theory of aging rests upon the gradual decline in the secretion of hormones which results in aging and decline in function and elevated mortality.

Estrogen, the predominant sex hormone in females, exerts considerable control over metallic metals in the body.

For example, cardiovascular disease (CVD) is the leading cause of death in the United States. The incidence of CVD is lower in premenopausal women than in men; however, CVD risk in postmenopausal women is 3.4 times that in premenopausal women. These differences in risk may be partially related to increases in excess body iron.[68] Iron stores increase with age in both men and women, paralleling the rise in CVD risk.

Estrogen releases metallic minerals from storage proteins to help grow babies. However, when the childbearing years are completed, estrogen releases minerals that have no target recipient (onboard baby). Even though ovaries may cease production of estrogen in menopause, the adrenals and fatty cells continue to produce estrogen. Once metallic metals like copper, cobalt, nickel, lead, mercury, tin, and chromium are released by estrogen from

their storage and transport proteins, they can stimulate the growth of breast tumor cells via their ability to activate the estrogen receptor, the gateway for estrogen to enter cells.[69] The rate of breast cancer rises significantly in postmenopause, concurrent with the accumulation and release of iron.

Iron control

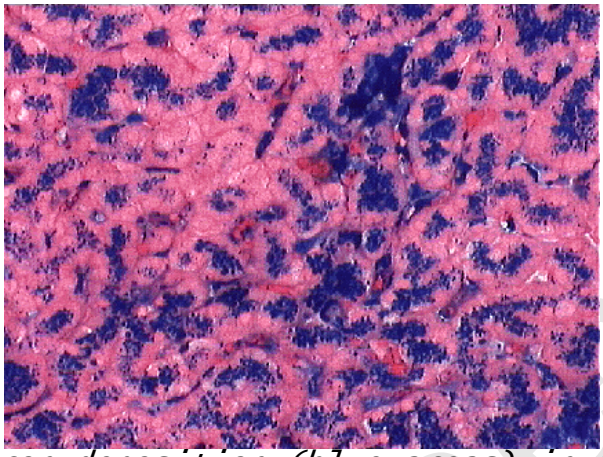
The human body has an elaborate system to control iron. Iron that is unbound, that is not attached to proteins (free iron), is the most dangerous form of iron. Unbound iron produces the hydroxyl radical, known as the most destructive species of free radical in the body. Indeed, oxidative injury is considered a major factor in accelerated aging.[70]

The majority of iron in the body is bound to the red hemoglobin pigment in red blood cells. As long as it is bound, it poses no problem. In a controlled fashion iron is transported to the bone marrow and dropped off for production of new red blood renewal.

Researchers in Japan have shown that young red blood cells have far less free iron than senescent red blood cells.[71]

Brown melanin pigment binds to iron in the skin. Neuromelanin binds iron in the brain. Albumin, hemoglobin and white blood cells bind to or carry iron in the blood circulation. The liver produces an iron storage protein (ferritin), transport protein (transferrin) and a protein

that is produced during infection (lactoferrin) to limit iron availability to germs during states of infection. Excess iron is stored in the liver.



Excess iron deposition (blue areas) in the liver

Dietary control of iron

Molecules in the diet also augment the control of iron in the body. What are known as polyphenols of bioflavonoids, metal-binding pigments found in the rind of citrus fruits, the skin and seeds of grapes, in berries and cherries and green tea, help to control copper and iron in the body. Polyphenols are better at controlling copper than iron.[72] Substances in fruits, grapes, berries and tea called polyphenols (flavonoids) provided in fruits, grapes, berries, wine and tea, are nature's way of helping the body control iron and copper-induced oxidation.[73]

Quercetin, a strong antioxidant in onions and red apples, is also a strong iron chelator.[74] Animal studies show that quercetin can release iron from storage in the liver of

animals, and the released iron is then excreted in the feces.[75]

The polyphenols in tea, and to a lesser extent coffee, actually decrease the absorption of iron considerably. For comparison, orange juice, by virtue of its acidity and vitamin C content, increases absorption of iron from foods by 85 percent.[76] Therefore, orange juice is a beverage that should be preferred during the growing years to enhance growth via the availability of iron. Tea, wine and whole grains are the preferred beverages to slow down aging and reduce the risk of disease after age 18 for males and with the onset of menopause in females.

Green tea, more so than black tea, binds to copper and prevents its accumulation. Green tea prevents DNA mutation, tumors and elevation of cholesterol via its ability to bind to metallic minerals.[77]

When copper is added as an oxidizing agent, the addition of red wine components to cholesterol particles in a laboratory dish inhibits the oxidation (hardening) of the cholesterol by 4-fold compared to synthetic vitamin E.[78] Resveratrol, a red wine molecule, exhibits remarkable ability, at moderate dietary doses, to chelate and control copper, thus reducing oxidation (hardening) of cholesterol induced by unbound copper in the body. Resveratrol is superior in this regard to other polyphenols (bioflavonoids). However, resveratrol does not chelate iron.[79]

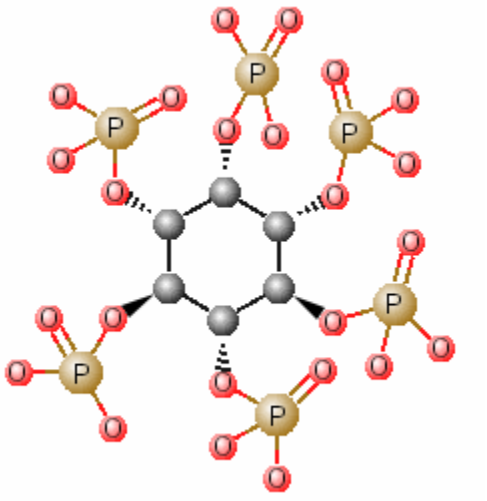
Red wine components do not induce deficiencies of copper or zinc. They appear to counter negative health effects of copper after they are absorbed.[80]

Resveratrol, as an extract from wine skin, is a stronger inhibitor of oxidation (hardening) of cholesterol than plain red wine skin powder (no extraction).[81]

Resveratrol works at very low concentrations. A grape extract diluted 8000 times was still able to inhibit the hardening of cholesterol in a laboratory study.[82]

The Sirtuin 1 gene is a DNA repair gene that is activated by resveratrol.[83] DNA repair, including repair of double-strand DNA breaks, is accelerated when cells are exposed to resveratrol.[84]

Phytate from rice bran



IP6 phytate molecule
(Inositol + 6 phosphorus molecules)

The major iron-controlling molecule in the human diet is phytic acid, found in bran, whole grains and seeds.[85] Phytic acid-IP6 is widely known for its anti-cancer properties.[86]

Phytate IP6 also addresses the antioxidant theory of aging by reducing oxygen free radicals. About 2 percent of oxygen molecules will loss an electron and become a tissue-destructive free radical. This means an estimated 20 billion oxygen free radicals will be produced daily. Phytate IP6 reduces oxidative damage in the body by (1) removal of iron; (2) attachment to free unbound iron; (3) removal of iron stores, such as from the liver; (4) and more uniquely, by reducing oxygen affinity to red blood cells. If fewer oxygen molecules are being delivered to tissues, oxygen free-radical production is reduced. Red blood cells survive longer when modified by phytate IP6.[87]

It is interesting to note that the Food & Drug Administration approved health claims for soy protein in 1999 as a food that reduces the risk for heart disease. But the ingredients in soy that produce this health benefit were not identified at the time. Subsequent studies reveal an iron-controlling molecule abundant in soy, phytate IP6, is what produces the cardiovascular health benefits in soy protein, not the widely touted weak estrogen-like molecules (phytoestrogens) in soy.[88]

Phytic acid is misunderstood by dieticians. It has been mischaracterized as an anti-nutrient that impairs the absorption of iron, copper, and other essential metallic

minerals, inducing anemias (shortages of iron, copper, etc). Dieticians often recommend phytic acid be removed from foods as it impairs growth during childhood and may contribute to anemia among fertile women. However, the need for metallic minerals is greater during childhood and by menstruating and pregnant females. Phytic acid needs re-evaluation. It is an important molecule in the control of iron-induced disease throughout the body.[89]

Phytate IP6 inhibits and reverses calcification

The iron-chelating properties of phytate IP6 have overshadowed its ability to chelate calcium. Phytate IP6 also has strong calcium chelating properties. Phytate IP6 can inhibit crystallization of calcium crystals and clear calcium deposits from kidneys (kidney stones).[90] Phytate IP6 inhibits calcifications in the cardiovascular system.[91]

Telomeres are end caps on chromosomes.
The shortening of telomeres correlates with aging.

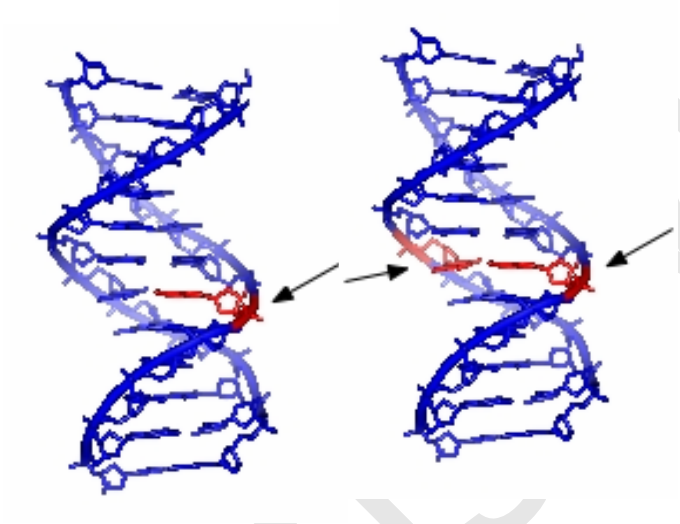
Telomeres and IP6

Another theory of aging is also addressed by phytate IP6. As they age, cells begin to become shorter. The end caps, or telomeres, on germ cells, stem cells, and most cancer

cells are progressively shortened with advancing age. The telomere theory of aging rests on the discovery that telomeres shorten each time a cell divides. The enzyme telomerase is critical for this shortening process, which also induces immortality to cancer cells. It has been shown that phytate IP6 represses the activation of telomerase and thus prevents cancer cells from becoming immortal.[92]

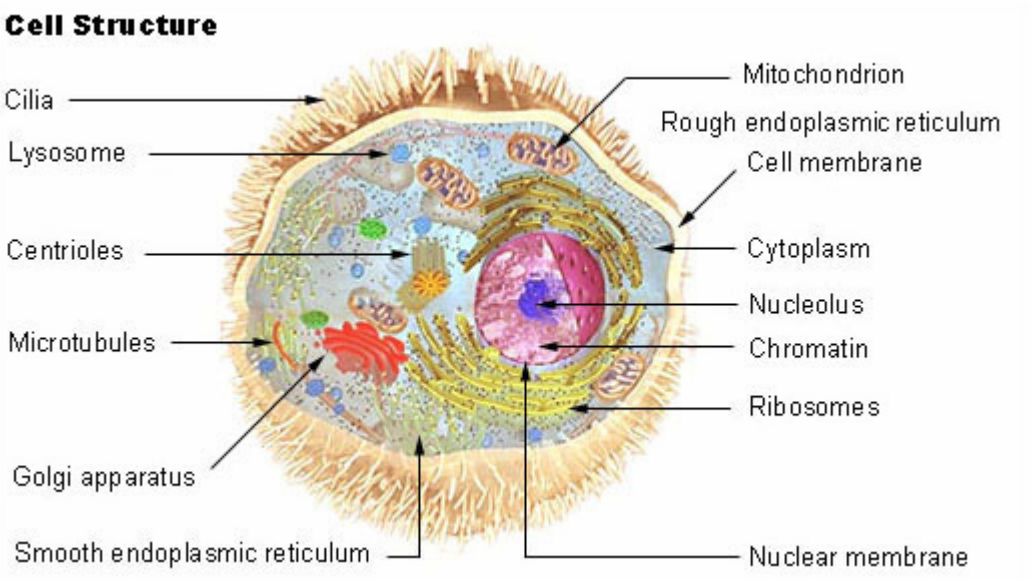
Resveratrol also inhibits telomerase effectively.[93]

Phytate IP6 and DNA repair



Single strand DNA break (left) and double-strand DNA break (right)

DNA damage is proposed by some biologists as the primary cause of aging.[94] Breaks in DNA must be repaired. For the longest time researchers could not determine how a double-strand DNA break is repaired. Only recently has it been determined that phytate IP6 facilitates stimulation of the joining of complementary ends of DNA in double-stand DNA breaks. This makes phytate IP6 critical for cellular repair and longevity.[95]



Overmineralization and the mitochondrial theory of aging

Mitochondrial dysfunction is considered one of the earliest changes that predict the onset of disease and premature aging.[96]

Overmineralization of mitochondria, the energy-producing compartments with living cells, is involved in the aging and death of mitochondria and the rate of aging in the entire body.

Mitochondria are miniature thread-like organs within living cells. The mitochondria produce up to 80% of cellular energy needs. To produce energy, the mitochondria use as fuel more than 90 percent of the oxygen that a person inhales. The mitochondria are also where 95 percent of the oxidation or rusting occurs within the body.

A brief description of the role of the mitochondria in the body is in order. There may be 20-2500 mitochondria in

each human cell in the body. They produce the energy for muscle activity, heart pumping, breathing, brain function, etc. More than 90% of all the oxidation that occurs in the body occurs within the mitochondria.[97]

Finding the biological clock: it's in the mitochondria

In 1972 Denham Harman first suggested that the mitochondria might be the biological clock for the body. Later, in 1980 J. Miquel proposed the mitochondrial theory of aging. The production rate of *"rusting agents"* (iron and oxygen induced free radicals) within the mitochondria correlate with the maximal life span of any species of life. Mitochondrial oxidation in females is significantly lower than males, which may help explain why females outlive males.[98]

Mitochondrial DNA

The DNA genetic material in the mitochondria is more vulnerable to damage than DNA in the nucleus of cells. DNA in the cell nucleus is protected by virtue of its wrapping around histone bodies (like thread around a spool). But mitochondrial DNA has no such protection. Oxidative damage to DNA in the mitochondria is many times greater than DNA in the cell nucleus. By age 90 only about 5% of the mitochondrial DNA is intact in a male.[99]

Researchers at the Karolinska Institute in Stockholm, Sweden, report that mutations in mitochondrial DNA have a causal relationship with aging in mammals. When mice are engineered to carry a damaged version of a mitochondrial

enzyme, damage in the mitochondria increases 3-fold and by 25 weeks of age, which is young adulthood for rodents, the mutations begin to emanate into visible signs of aging -- baldness, heart problems, bone thinning and reduced fertility. None of the animals lived beyond 60 weeks when healthy mice live 100 weeks on average.[100]

It's amazing that these small cell bodies exert so much control over aging. Mitochondria die off or exhibit mutation rates in a programmed fashion, accelerated by production of oxygen free-radicals. By slowing down or even switching this programmed death off, it's possible aging itself can be slowed.[101]

What causes all this trouble in the mitochondria with advancing age? -- the accumulation of iron and calcium. Iron deposition in the mitochondria is a unifying theory of aging.[102] The major free radical produced within the mitochondria is the superoxide radical, which releases iron from binding proteins.

The chelation (removal) of iron and calcium has been proposed as an anti-aging strategy in the mitochondria.[103]

Lipofuscin, an aging pigment that impairs cellular function, can form within the mitochondria due to the iron-induced oxidation of cellular debris. Chelation of iron would reverse or stop lipofuscin formation.[104]

Another theory of aging: cell cleansing

Another overlapping theory of aging is the *"cell cleansing"* theory. Living cells must rid themselves of debris. Cell bodies called lysosomes literally digest and recycle cellular debris, a process that even provides a source of cellular energy (food) in the event of starvation.

This cellular cleansing process is called autophagy. Activation of autophagy can increase longevity.[105] With advancing age, the garbage-digesting lysosomes and the energy-producing mitochondria in living cells eventually become burdened with excessive iron and calcium as well as other metallic minerals. Aged lysomes progressively fail to perform cell cleansing chores and the cell dies.[106]

The failure of the lysosomes to continually cleanse cells of debris is now considered a form of programmed cell death.

The failure of cells to cleanse themselves of debris is also associated with the occurrence of tumors.[107]

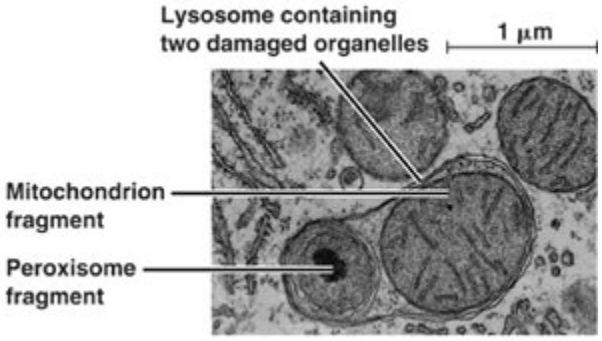
Both lysosomes and mitochondria are vulnerable to oxidative stress induced by iron.[108]

Calorie restriction is known to activate autophagy (cell cleansing).[109] Near starvation of animals increases autophagy and longevity.

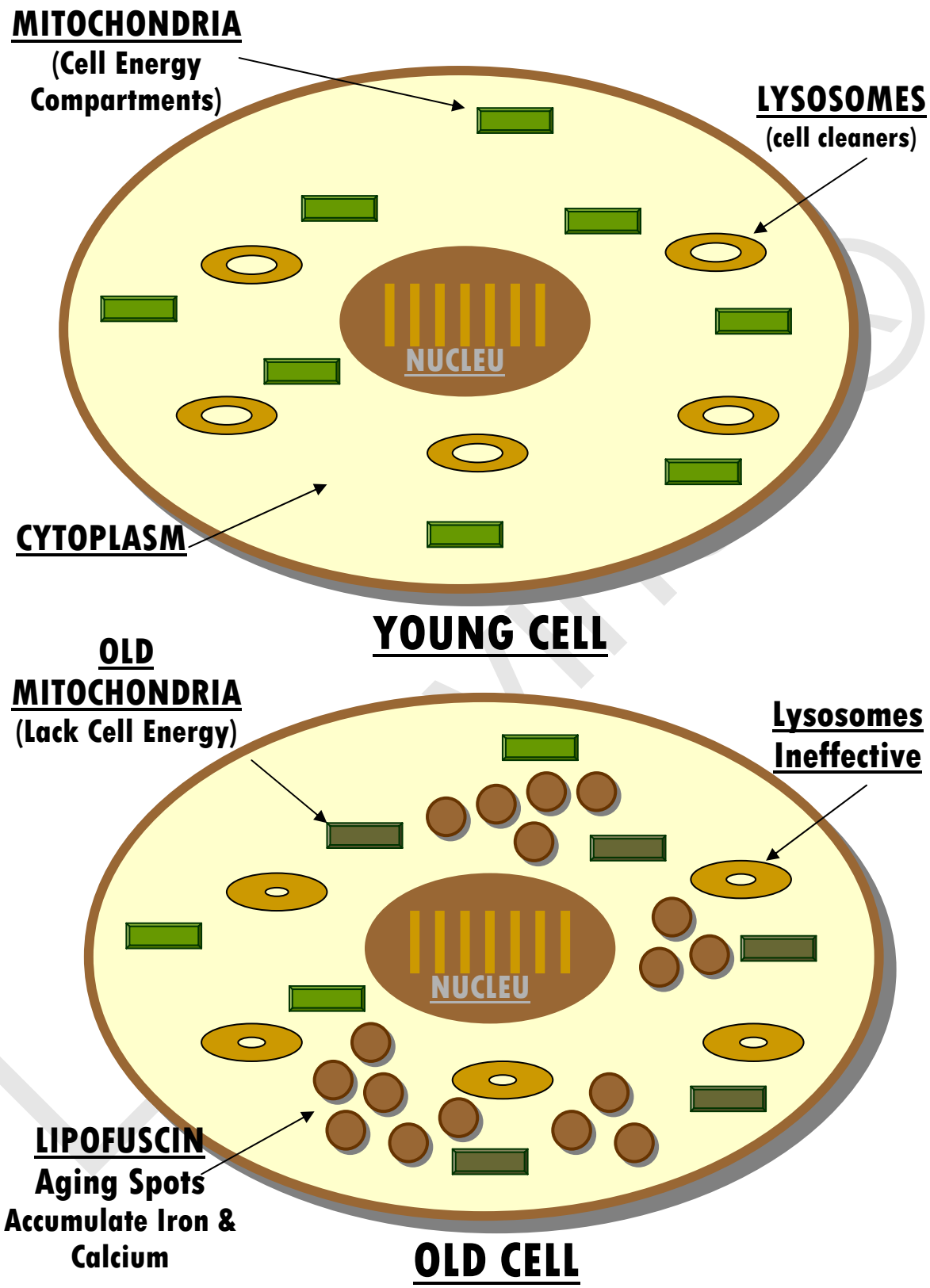
The use of iron chelators has also been shown to reverse the accumulation of cellular debris within aged cells, in a similar manner to calorie restriction.[110]

Iron chelation also reverses the progressive rupture of lysosomes and prolongs the life of cells.[111]

It is interesting to note that resveratrol activates autophagy (cell cleansing), which can either prolong the life of healthy cells, or shorten the life of tumor cells.[112] Phyate IP6, being an iron chelator, would also be anticipated to increase cell cleansing via autophagy.



Graphic showing a lysosome that has enzymatically "digested" two damaged parts of a living cell (damaged mitochondria and peroxisome).



Botanicals and the mitochondria

Natural molecules can play a strong role in protecting the mitochondria from oxidative damage.

For example, the DNA damage caused within the mitochondria is primarily caused by the superoxide radical.[113] Resveratrol inhibits the formation of the superoxide radical.[114]

Resveratrol has been shown to oppose the production of free radicals that cause mutations in the mitochondria.[115] Furthermore, resveratrol works in multiple ways to preserve mitochondria from damage.[116]

Phytate IP6 has also been shown to regulate the influx of calcium into mitochondria, thus protecting mitochondria from oxidative damage.[117]

Resveratrol and iron

While resveratrol is not a direct iron chelator, it does exert control over iron in living tissues via the production of an enzyme called heme oxygenase. Mice bred so they cannot produce heme oxygenase accumulate dangerous levels of iron in different organs. Resveratrol activates heme oxygenase activity, which controls iron and therefore prevents damage and aging in living tissues.[118]

The miracle of resveratrol is that it activates production of heme oxygenase in the brain and heart before events such as strokes and heart attacks occur. Otherwise, heme oxygenase is upregulated only after such events. This is

a remarkable *"pre-conditioning effect"* that serves to prevent damage to brain and heart tissues.[119]

Final corroboration: why aging ceases late in life

As final corroboration of the overmineralization theory of aging, an astounding and unexpected discovery was announced in 1992 – that aging ceases in late life. There is a flattening of the death rate late in adult life in many species (insects, worms, yeasts) and humans. At the greatest ages, mortality rates actually may decline.[120,121,122,123]

Lame attempts have been made to explain why aging ceases in the very old.[124]

No one made much of this discovery, announced in 1992 and it has remained an inexplicable phenomenon, till now.

"The discovery that aging ceases is one the most significant discoveries in recent aging research, with potentially revolutionary implications," says Michael R. Rose and colleagues at the Department of Ecology and Evolutionary Biology, University of California, Irvine.[125]

This discovery casts doubt on the idea that species have absolute life-span limits.[126]

The cessation of aging in advanced stages of life can be correlated with the cessation of iron accumulation in the very old. Males accumulate iron till middle age. Females only begin to accumulate iron with cessation of menstruation (menopause or early hysterectomy).

A 10-year study of adults who ranged in age from 60-93 years shows that iron storage levels (as measured by ferritin, a protein made in the liver that carries iron), level off and do not continue to rise in this age group. This is called *"achieving a steady state level"* of iron, that is, iron absorption is thought to be limited to amounts required to match that necessary to replace losses. The age at which an individual achieves his or her theoretical setpoint of iron stores has not been determined.

Dietary iron intake up to 10 milligrams achieves iron adequacy without inducing anemia. Iron supplements providing 18 milligrams of iron continue to add to the iron load of an individual at this age.[127]

The drawback of the above human study was that ferritin, the storage protein for iron, is often elevated in humans from chronic infection, inflammation or disease, which can result in misleading numbers. So researchers at Pennsylvania State University sought to validate the idea that iron reaches a steady state of storage in advanced age by conducting a controlled animal experiment. They found that old rats had significantly lower hemoglobin and blood plasma iron levels than middle-age rats, and lower total iron content in liver, spleen and bone marrow.[128]

Iron-Related Blood Measures Decline in Old Age

Age of rats	Hemoglobin, *g/l*	Plasma iron, *µmol/l*
Middle-aged rats	186.1	42.9
Old rats	147.8	23.2

Iron Content of Various Tissues of Old and Middle-Age Rats

µmol = micromolar concentration

	Liver iron		Spleen iron		Femur marrow iron	
Age of rats	*Concentration µmol*	*µmol/gram* wet tissue	*Concentration µmol*	*µmol/gram* wet tissue	*Concentration µmol*	*µmol/gram* wet tissue
Middle-aged rats	57.59	2.98	11.23	13.53	0.11	2.90
Old rats	23.36	1.40	7.35	4.56	0.07	1.20

Summary and conclusions

The overmineralization theory of aging helps to explain, and appears to be a predominant if not controlling factor, over the hormonal, oxidation and mitochondrial theories of aging. Overmineralization also is involved in the decline in melatonin production with advancing age. The pineal gland that secretes melatonin is considered the body's biological synchronizing clock.

Iron has been called the *"malignant spirit of successful aging."*[129] Iron deprivation has been proposed as an anti-aging strategy.[130] Barbara S. Polla, a researcher with the Latoratoire de Physiologie Respiratoire in Paris, France says that *"moderate iron deprivation might shortly add to other anti-aging 'miracles'"* and that iron chelators may *"shortly become the most efficient and fashionable*

antioxidant, anti-aging, anti-infectious, and anti-inflammatory therapy." [131]

Iron control appears to prolong or shorten the lifespan of many life forms. It is interesting to note that a gene that regulates senescence in wheat grain controls the iron and zinc content of the grain.[132]

Calorie restriction and molecular mimetics

Calorie restriction and its molecular mimic resveratrol have received much attention recently as anti-aging strategies. Calorie restriction is considered an unequivocal approach to prolonging life in all organisms. Seventy years of study confirms that calorie restriction decreases the rate of aging by lowering the generation of free radicals in the mitochondria of cells.[133]

The key experiment, presented earlier in this paper, conducted by researchers at McGill University in Canada, conclusively showed that dietary restriction did NOT reduce the number of aging deposits in brain tissues compared to rats fed a normal diet, but did reduce aging deposits in the brain when a standard calorie-restricted diet with low metallic mineral content was compared against a diet where animals ate a restricted-calorie diet with added metallic minerals.[51] It's the minerals, not the calories, that control aging.

From a gene-switching standpoint, calorie restriction activates the Sirtuin 1 gene, which increases the life span of many organisms.[134]

When the question arose, could the Sirtuin 1 gene, activated by calorie restriction, also be activated molecularly without food deprivation,[135] researchers were quick to answer the question. Resveratrol, a red wine molecule, has now been identified as a molecular mimic of calorie restriction and activator of the Sirtuin 1 DNA repair gene.[136]

The health benefits of calorie restriction mimics are not new. The French, by virtue of their traditional consumption of red wine, have been activating the Sirtuin 1 gene for some time. The French live 45-65% longer in wine-growing districts.[137]

There is even the meticulously documented presentation of a man, Luigi Cornaro, who lived in Padua, Italy over 500 years ago, who limited his food intake to 12 ounces, and wine intake to 3 glasses per day, and lived 102 years.[138]

Luigi Cornaro (1464-1566 AD), of Padua, Italy, preceded recent discoveries that calorie restriction and red wine resveratrol can prolong human life, by limiting intake of food to 12 ounces, and red wine to 3 glasses per day,and lived 102 years in excellent health to his dying day.

Even though the French utilize a dietary source of resveratrol and benefit with leaner bodies and lower cardiovascular mortality rates from the traditional

consumption of red wine, the drawback of alcohol and calories in wine can be overcome with a red wine pill. So we now live in an era of calorie restriction mimics.[139]

Resveratrol, the molecular mimic of calorie restriction, appears ready to make its impact upon human health as a dietary supplement. While resveratrol will continue to captivate scientists and the public, it is not the only life-prolonging molecule nature provides.

Recent discoveries involving gene switching with small molecules like resveratrol should not overshadow the overmineralization theory of aging and the advantage of a broader array of mineral chelators, such as phytate IP6 and quercetin, to waylay aging. (Subject of an applied-for patent.)

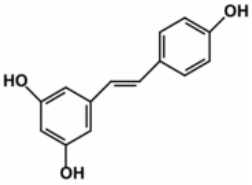
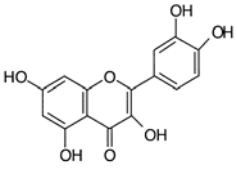
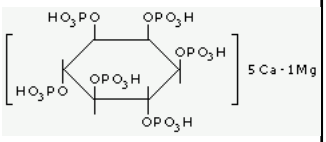
Other recent efforts have already been made to unify the many theories of aging.[140] This paper broadens the understanding of life extension even more.

Longevinex® provides a unique array of mineral chelating ingredients, resveratrol, quercetin and phytate IP6, that address the accumulation of iron, copper, calcium and other heavy metals in the human body with advancing age.

MINERAL CHELATORS IN LONGEVINEX®		
INGREDIENT	CHELATES (binds to)	NATURAL SOURCE
Resveratrol*	Copper	Red wine grapes, Giant knotweed
Phytate (IP6) bran factor	Iron, copper, calcium, heavy metals	Rice bran
Quercetin	Iron	Onions
* Resveratrol exerts control over iron by activation of an iron-controlling enzyme called heme oxygenase		

Synergism of Molecules in Longevinex®

Polyphenols are small molecules found in nature. Polyphenols do not work solely by themselves, but rather in league with other polyphenols

Trans Resveratrol	Quercetin	IP6 rice bran	Lecithin
			
			CH2OR1 - CHOR2 · CH2OPO - OHR3
228 molecular weight	302 molecular weight	698 molecular weight	--
Sirtuin 1 gene activator (DNA repair gene; copper chelator; anti-fungal, anti-viral, anti-inflammatory	Sirtuin 1 gene activator; allows immediate use of resveratrol; anti-viral; antihistamine	Iron and metallic metal chelator; antoxidant stabilizer; required to repair double-strand DNA breaks	Emulsifier; facilitates absorption, entry through cell walls, entry to blood brain barrier

Addendum 2

Another report on how ingredients in Longevinex® inhibit or even reverse human aging

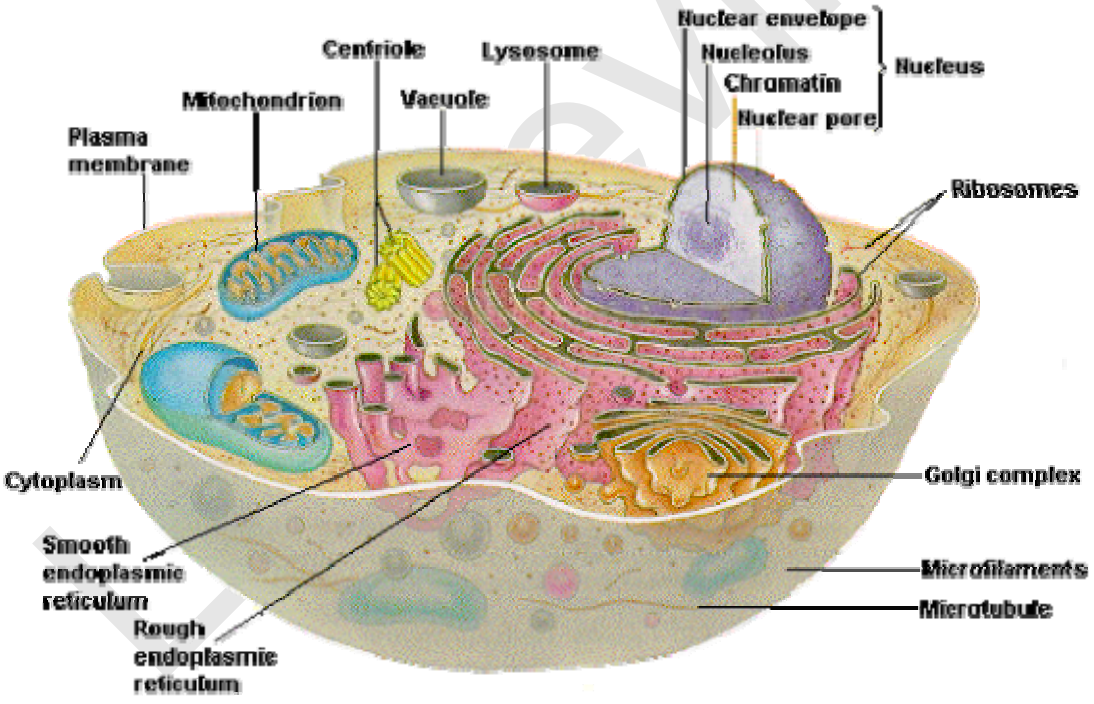
Cellular protein degradation and removal in aging

By Bill Sardi

Living tissue cells, all 10 trillion of them in an average sized human, must cleanse and renew themselves from within to remain functional. This cleansing process becomes increasingly less efficient with advancing age.

As aging proceeds there is an overload of damaged proteins that must be cleared from cells. Without clearance of these damaged cell parts, there is destabilization of cells and aging. In an 80-year old human about half of all proteins are oxidized.[141]

Structures inside living cells called **lysosomes**, which produce enzymes, perform cellular cleanup. Researchers have studied how cellular debris, fats, proteins, etc., gets delivered to **lysosomes**.



Cellular debris must make its way through a labyrinth-like structure within cells, called the **endoplasmic reticulum**, to lysosomes, which digest the cellular garbage.

Old cells accumulate undegraded products. One of these garbage deposits is **lipofuscin**, considered a marker of aging. Lipofuscin increases with age in living tissues. Here is the progressive increase of lipofuscin among senior adults, in lymphocytes (white blood cell in lymph):[142]

	Age 60-69	Age 70-79	Age 80-89	Centenarians
% Lipofuscin	11%	14%	18%	62%

As undegraded proteins and fats accumulate they begin to crosslink molecularly until they become indigestible. So the earlier anti-aging strategies are employed the better.

Starvation and cellular debris

Biologists have discovered that starving cells rid themselves of debris better than well-fed cells. This may be why calorie restricted diets result in longer lifespans. But even starving cells cannot get rid of lipofuscin very well.

In 1995 it was proposed that **autophagy** is responsible, in part, for the anti-aging effects of calorie restriction. (Autophagy is a term used to describe digestion of debris within cells.) Extensive evidence now supports this theory. During nutrient starvation increased levels of autophagy lead to the breakdown of non-vital components and the release of nutrients, ensuring that vital processes can continue.[143]

There is inceasing evidence that damage to proteins, DNA, cell wall lipids (fats), and organelles within cells are an important factor in aging. A decline in the ability of lysosomes to degrade and digest broken cellular components is at the heart of the aging process.[144]

Cellular debris that cannot be efficiently removed is more likely to accumulate in cells that have slower cell replacement rates, such as those in the brain, eyes, heart and muscle fibers. Therefore, these tissues are more likely to age before others in the human body.

Works by lowering insulin levels

By maintaining blood plasma levels of **insulin** at markedly lower levels during long periods of fasting throughout life, calorie restriction increases autophagy, or the cleansing of cells. Treatment with insulin reverses some of the beneficial anti-aging effects of calorie restriction.[145]

Autophagy and infection

Autophagy also kills bacteria in living cells. Intracellular pathogens such as *Mycobacterium tuberculosis* persist within cells and block the normal actions taken by the cell to rid itself of it.

Stimulating autophagy in infected cells overcomes the block and helps to rid the cell of pathogens.[146]

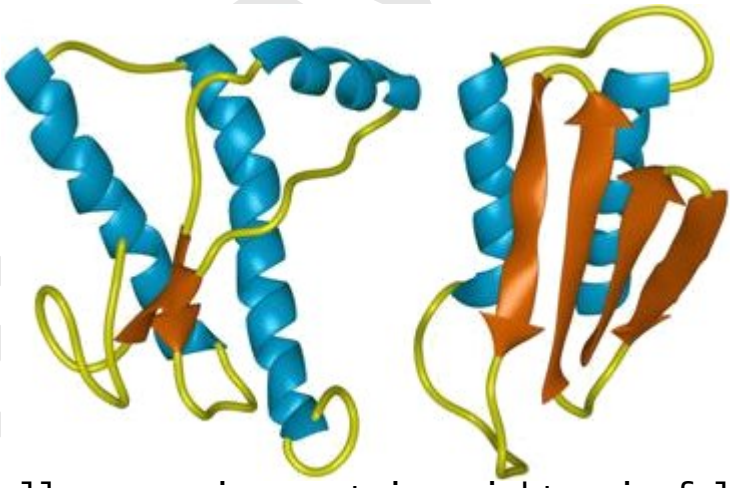
Autophagy and cancer resistance

Furthermore, there is an interesting link between longevity and resistance to cancer has been made, which correlates with cellular housekeeping facilitated by **molecular chaperones**. The silencing of genes involved in cellular cleanup contributes to the decrease in cancer resistance.[147]

Iron, oxygen and lipofuscin

In lab experiments, an increase in **iron** or **oxygen** (40% ambient oxygen, vs. 21% normal oxygen content) will increase oxidation and result in lipofuscin formation, whereas growth at lower levels of oxygen (8%) and treatment with antioxidants or iron-chelators diminishes lipofuscin formation. Researchers believe lipofuscin forms within lysosomes as a consequence of iron-induced oxidation of cellular debris. The control and chelation (removal) of excess iron and oxygen is of great importance in slowing or reversing the aging process. The dietary provision of a key iron/oxygen-controlling molecule found in whole grains, IP6 phytate from bran, is unique here. It is the only molecule in nature that reduces the affinity of oxygen to red blood cells as well as chelates (attaches to) loose iron.[148]

Molecular chaperones and protein folding



Left, naturally-occurring protein; right, mis-folded protein

Molecular chaperones and autophagy

One way cellular debris is delivered to lysosomes is via what is called *"chaperone-mediated autophagy."* Chemical chaperones function to stabilize improperly folded proteins and to facilitate their transport more efficiently toward lysosomes that digest these proteins. Chaperones (also called *"**heat shock proteins**")* also

inhibit oxidation and stickiness of proteins, something called crosslinking.[149] Chaperone function decreases with advancing age.

Chaperone function decreases with advancing age. Toxic compounds and nutritional shortages or overages activate chaperone-mediated autophagy.

Impaired chaperone function may also emanate from chaperone overload. The balance between misfolded proteins is disturbed and chaperones in advanced age.[150]

Chaperone-mediated autophagy is activated by prolonged starvation. Researchers now postulate that the everyday administration of calorie restriction mimics, as stimulators of chaperone-mediated autophagy, may offset aging and the onset of age-related diseases.[151]

Because molecular chaperones function inside living cells, they must be small molecules that can navigate within the intracellular organelles, like the endoplasmic reticulum.[152]

Resveratrol, as a small-molecular mimic of calorie restriction, is currently the most studied molecule for the purpose of slowing or reversing the aging process.[153] Resveratrol has been shown to protect against endoplasmic reticulum stress and cell death. [154]

What all this means is that cellular aging precedes disease by many decades. This decades-long time period would give humans an opportunity to slow the biological clock-hands of time, if such cell cleansing mechanisms can be identified and employed. Even reversal of aging at an advanced age may be possible.

Loss of ocular transparency indicative of speed of aging

Of notable interest is the recent published report which indicates stress in the endoplasmic reticulum of living cells, which induce an unfolded protein response, results in reactive oxygen species in cells within the focusing lens of the human eye. This oxidative stress can lead to the onset of cloudy cataracts that obscures vision and reduces delivery of focused light to the back of the eyes. Cataracts are an age-related disease. Therefore, even the slightest lens opacity (cataract) in young patients might serve as a marker of systemic aging.[155] The early use of a meter to measure the progressive decline in light transparency through the lens of the eyes with advancing age might be a way of non-invasively determining the speed of biological aging.[156]

Addendum B

Naked mole rat controls minerals to achieve super longevity; consistent with overmineralization theory of aging

The naked mole rat continues to astound researchers. It outlives other rodents by far. By comparison, mice live about 3-3.5 years, guinea pigs 6 years, and naked mole rats up to 28 years. One of these subterranean animals (they live their lives underground) was captured in Kenya in 1974 and lived in an animal lab till 2002. [Science Aging Knowledge Environment 2002: 7, 2002] In the animal lab, many are alive after more than 20 years and some are 26 years old (and counting), which is older than the maximum longevity of all but one of 156 rodent species that have been maintained in captivity from birth to death. [Journal Zoology 258: 307-11, 2002]

A theory of aging is that oxidation, the progressive production of destructive oxygen and iron species in living tissues with advancing age, results in accelerated aging. However, the naked mole rat defies this definition of aging. Tissues obtained from the naked mole rat surprisingly show, even at a young age, markers of oxidation and iron are at least twofold greater in naked mole rats than in mice. This refutes the hypothesis that prolonged naked mole-rat longevity is due to superior protection against oxidative stress.
[Aging Cell 5: 525-532, 2006]

While researchers express their puzzlement over this animal's long life span, careful study reveals this animal has unusual ways to control minerals in its body and therefore outlives other rodents.

The naked mole rat achieves unusual longevity in the following ways:

1. Only the breeders live exceptionally long. The worker mole rats only live about 3.5 years, about as long as other rodents. A queen mole rat produces offspring throughout life and can produce 100 pups a year, even in her twenties. This means iron and calcium iare constantly being shuttled from mother to offspring and thus prevents mineral overload in the mother mole rat. This is why female humans outlive males – they control mineralization via monthly menstrual flow and donation to offspring, and outlive males by 5-8 years, on average.
2. The naked mole rat's ever-growing teeth are constantly being worn down during digging and researchers believe their teeth represent a *"mineral sink."* This is similar to the way a deer or moose prevents calcifications by accumulating minerals in its antlers and then shedding them seasonally. [General Comparative Endocrinology 81: 500-05, 1991.

Longevinex proposes human aging begins when full-growth is achieved, at around age 18 years. Prior to that time calcium and iron are being shuttled to produce new bone and red blood cells. Once full growth is achieved, the human body begins to accumulate excessive amounts of calcium and iron that begin to calcify and rust living cells, resulting in malfunction of mitochondria and lysosomes in living cells that are responsible for producing cell energy and removal of cellular debris. Longevinex is a unique combination of plant extracts designed to chelate (attach to and remove) excess amounts of calcium, iron, copper and heavy metals from aging tissues. –Copyright Longevinex 2007.

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