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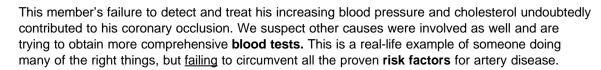
REPORT

How to Circumvent 17 Independent Heart Attack Risk Factors

By William Faloon

One of our most enthusiastic members just sent me a dismaying email. After a sudden **angina** attack, this 64-year-old man was diagnosed with severe **coronary artery blockage**. His doctors ordered bypass surgery. Based on the severity of his coronary blockage, surgery was his only option.

Since this member lived in rural England, **comprehensive blood tests** were not readily available to him. The best that socialized British medicine provided was a report showing that he had <u>high</u> **cholesterol** and very <u>high</u> **blood pressure**. A review of his supplement program revealed gaping holes in what we know is needed to protect against **atherosclerosis**.





Atherosclerosis was once considered an inevitable consequence of aging. The problem now is that too many people think they can protect against heart attack by picking and choosing among various components of an anti-atherosclerosis program.

From our observations over the past **29 years**, I can categorically state that <u>without</u> **annual blood tests** (and regular blood pressure checks), an aging human is literally shooting in the dark if they think they can avoid contracting a vascular disease.

Today's population remains in a virtual state of denial when it comes to **heart attack** risk. What makes this such a travesty is that there are so many **proven** ways to protect against the number one killer. This article will succinctly review <u>17</u> independent **heart attack risk factors** and provide a range of options that can enable aging humans to defuse each one of them.

The order in which I discuss these **cardiac risk factors** has no relevance as to which is more dangerous than the other. It does not matter if your fatal heart attack is caused by high cholesterol, low testosterone, or excess glucose—the end result may be the same, unless all of these risk factors are brought under control.

The encouraging news is that simple steps that enable one to lower risk factors such as elevated **LDL** simultaneously protect against other dangers such as excess **C-reactive protein**.

HEART ATTACK RISK FACTORS #1 and 2: Excess LDL and Total Cholesterol

OPTIMAL BLOOD LEVEL:

160-180 mg/dL of total cholesterol 50-99 mg/dL of LDL (low-density lipoprotein)

Low-density lipoprotein (LDL) transports **cholesterol** from the liver to cells throughout the body, where the cholesterol provides numerous life-sustaining functions. As people age and/or consume the wrong foods, LDL and cholesterol levels tend to increase to a point whereby they cause or contribute to the development of atherosclerosis. It is thus important to maintain total cholesterol and LDL levels in *optimal* ranges.

Drug options: Take the lowest dose of a **statin** drug that achieves optimal LDL and total cholesterol levels. Some people will need only **5-10 mg** of **simvastatin** or **20-40 mg** of **pravastatin** per day. These low doses seldom cause side effects, other than to reduce coenzyme Q10 (CoQ10) synthesis in the body. Supplemental CoQ10 can correct a CoQ10 deficiency caused by statin

drugs.1,2 Many people can avoid statin drugs by making dietary changes and incorporating certain nutrients and fibers into their daily program.

NUTRIENT OPTIONS:

- 1. **Niacin** in doses of **1,000-2,000 mg** a day will significantly lower total cholesterol, LDL, and triglycerides while boosting beneficial high-density lipoprotein (HDL).3-8 Niacin can cause a skin "flushing" side effect that can be mitigated by taking niacin with aspirin and a meal. Some people cannot tolerate this flushing effect on a daily basis and choose other options to lower LDL and cholesterol.
- 2. A patent-pending extract of **Indian gooseberry fruit** called **Amlamax®** has been shown in human clinical trials to reduce LDL, total cholesterol, triglycerides, and C-reactive protein (CRP).9-14 Amlamax® has also been shown to improve endothelial function.15,16 The suggested dose is **380-500 mg** each day.
- 3. The liver removes cholesterol from the blood and excretes much of it into the small intestines in the form of bile acids. If these bile acids are reabsorbed from the intestines back into the blood, then too much cholesterol can accumulate in the blood and contribute to atherosclerosis. The ingestion of soluble fiber(s) such as **oat beta-glucan**,17-19 **psyllium**,20 **guar gum**,21,22 **pectin**,23,24 and/or **glucomannan**25 can result in significant reductions in LDL, total cholesterol, and glucose. The most common way of using these fibers is to mix them in eight ounces of water and drink them before most meals. These fibers can also be taken in capsule form. Start off with relatively modest doses and slowly work up to higher amounts to enable your digestive tract to get used to this higher fiber intake. Depending on the type of soluble fiber you choose, taking **two** to **eight grams** (2,000-8,000 mg) before each meal is a reasonable target to attain.
- 4. Ingestion of **375 mg** a day of **theaflavins** extracted from black tea produces a modest reduction in LDL and total cholesterol.₂₆₋₂₈ The primary benefit of theaflavins is to suppress C-reactive protein and LDL oxidation involved in the formation of atherosclerotic plaque.
- 5. **Irvingia** extract, taken in the dose of **150** mg twice a day, is associated with beneficial changes in LDL and total cholesterol through reductions in weight and overall calorie intake.29-32

Dietary options:

- 1. Consume a **very low-fat diet** (less than 10% of total calories from fat). Make sure to supplement with at least 2,000 mg of EPA/DHA (omega-3 fats) each day. Most people cannot adhere to this kind of strict low-fat diet.
- Consume a very low-calorie diet (often less than 1,400 calories a day). Most people cannot adhere to a very low-calorie diet.33
- 3. Consume a **Mediterranean diet,** with lots of fresh fruits and vegetables, fish and soy as protein sources, and omega-3 and monounsaturated fats (olive oil), while avoiding saturated fats, refined carbohydrates, cholesterol-laden foods, excess omega-6 fats, and most animal products. An increasing percentage of Americans are adopting this kind of diet.34-37
- Inclusion of specific cholesterol-lowering foods in one's diet can markedly lower LDL and total cholesterol levels. Cholesterol-lowering foods with documented proven efficacy include almonds,38 soy protein,38 fiber,19,38 and plant sterols.38

Hormone options: Many women (and some men) suffer from excess cholesterol because they are deficient in thyroid hormone. Blood tests that evaluate TSH, T4, and T3 can help a qualified doctor restore thyroid hormone status to optimal ranges. Cholesterol is a precursor to testosterone and other hormones in the body. When testosterone is deficient in men, the body may compensate by synthesizing more cholesterol. When testosterone and other hormones are restored to more youthful ranges, cholesterol levels may decrease. Aging men sometimes have higher than desirable levels of estradiol._{39,40} Excess estrogen in men contributes to elevated LDL and cholesterol.₄₁ Elevated levels of estrogen can be suppressed in men by taking 0.5 mg twice a week of the prescription drug Arimidex®₄₂ or using nutrients like plant lignans (30 mg a day and higher of HMRTM Lignars)₄₄ and Bioperine®-enhanced absorption chrysin (1,500 mg a day).₄₅

WHAT YOU NEED TO KNOW: HOW TO CIRCUMVENT 17 INDEPENDENT CARDIOVASCULAR RISK FACTORS

- Annual blood testing and regular blood pressure screenings are the most important steps individuals can take to protect against vascular disease.
- Blood testing can reveal numerous cardiovascular risk factors including excess LDL and cholesterol, low HDL, excess glucose, high homocysteine, elevated CRP, high triglycerides, elevated fibrinogen, low vitamin D, excess insulin, and low testosterone and high estradiol (in men).
- Other common vascular risk factors associated with aging are high blood pressure, oxidized LDL, nitric oxide deficit, and insufficient vitamin K.
- If these risk factors are outside of optimal ranges, a range of dietary, nutrient, drug, and hormone therapies can be employed to help bring them into safe ranges.
- Addressing all 17 risk factors is essential for comprehensive cardiovascular risk reduction.

OPTIMAL BLOOD LEVEL:

Over 50-60 mg/dL of HDL

High-density lipoprotein **(HDL)** functions via several mechanisms to protect against atherosclerosis, including removing cholesterol from the arterial wall for disposal in the liver. The technical term for this removal of cholesterol is "reverse cholesterol transport." In order for optimal *reverse cholesterol transport* to occur, the blood should contain both enough HDL particles and factors that HDL requires to facilitate the **reverse cholesterol transport** process.



Drug options: Statin drugs provide only slight increases in HDL. The most effective drug to significantly increase HDL is called **Niaspan®**, a form of extended-release **niacin**. Niaspan® costs far more than niacin supplements, but may be better tolerated by some individuals. The potential danger of Niaspan® is that because of its continuous release, it may damage the liver. According to the manufacturer's website: "**Liver damage has been reported when substituting Niaspan® for immediate-release niacin."**46

NUTRIENT OPTIONS:

- 1. **Niacin** in doses of **2,000-3,000 mg** a day may be the most effective way to increase **HDL**, while simultaneously lowering total cholesterol, LDL, and triglycerides and inducing favorable changes in LDL particles to reduce their atherogenic potential._{3-8,47} Niacin can cause a skin "flushing" side effect that can be mitigated by taking niacin with aspirin and food. Some people cannot tolerate this flushing effect on a daily basis and choose other options to increase HDL.
- 2. A patent-pending extract of **Indian gooseberry fruit** called **Amlamax**® has been shown in human clinical trials to modestly increase **HDL**, while reducing LDL, total cholesterol, triglycerides, and C-reactive protein (CRP).9-14,48 The suggested dose is **380-500 mg** each day.
- 3. Paraoxonase-1 is an enzyme strongly associated with the anti-atherosclerotic <u>functionality</u> of HDL. When paraoxonase-1 is deficient, HDL oxidizes and is unable to perform its vital mission of removing cholesterol from the arterial wall. Low levels of paraoxonase-1 predict a substantially increased risk of extensive coronary artery disease, regardless of HDL <u>level</u>.49 In patients administered eight ounces of pomegranate juice a day, paraoxonase-1 levels increased by 83% after one year.50 The nutrient quercetin (in an absorbable form) also upregulates paraoxonase-1.51 Since paraoxonase-1 is not a readily available commercial blood test, those seeking to achieve ultimate HDL <u>functionality</u> should drink unsweetened 100% pomegranate juice and/or take 400-500 mg of standardized pomegranate supplements that provide the active constituents of eight ounces of pomegranate juice.

Dietary options: Eating the cruciferous vegetables **broccoli**, **watercress**, and **cabbage** may enhance HDL <u>functionality</u> via several mechanisms. Excess abdominal fat seems to contribute to low HDL. Losing weight and increasing physical activity can result in higher HDL levels by helping to reverse *metabolic syndrome*. Red wine can also have a profound impact on increasing HDL levels. One glass of red wine with your heaviest meal is suggested, as long as you can tolerate the alcohol.

Hormone options: When **HDL** removes cholesterol from the arterial wall, it is taken to the liver where it is broken down for disposal and transformed into beneficial compounds such as vitamin D. The liver contains a receptor called *scavenger receptor B1* that acts to stimulate cholesterol uptake for processing and disposal. The liver also has an enzyme called *hepatic lipase* that functions to remove cholesterol from the surface of HDL and helps enhance the uptake of these HDL-derived lipids by *scavenger receptor B1.*52,53 The activity of *scavenger receptor B1* and *hepatic lipase* is a crucial component of the **reverse cholesterol transport** process. **Testosterone** beneficially increases the activity of *scavenger receptor B1* and *hepatic lipase.*54 It is especially important for men to restore **testosterone** to youthful levels in order to ensure that the cholesterol that HDL removes from the arterial wall is safely disposed in the liver. Men with pre-existing prostate cancer should avoid testosterone until their cancer is cured.

HEART ATTACK RISK FACTOR #4: Excess Glucose

OPTIMAL BLOOD LEVEL:

Under 86 mg/dL of fasting glucose

Back when *Life Extension* started making disease risk-reduction recommendations, the medical establishment thought fasting glucose levels up to **125** mg/dL were acceptable. The establishment soon reduced its upper acceptable limit to **110** mg/dL. In

recent years, it has come to believe that 100 mg/dL of fasting glucose is too high.

Scientific studies indicate that any amount of fasting glucose over **85** mg/dL incrementally adds to heart attack risk.55 In fact, if you can choose an absolute ideal fasting glucose number, it would probably be around **74** mg/dL.56 We know that some people are challenged to keep their glucose under **100** mg/dL, which makes following as many steps as possible to suppress blood glucose especially important. The good news is that many of the approaches to reduce fasting glucose also reduce fasting insulin, LDL, total cholesterol, and C-reactive protein.

Drug options: An antidiabetic drug that *Life Extension* suggests normal aging people consider taking to lower their fasting **glucose** level is **metformin**, and it is available in low-cost generic form. Metformin has a long enough history of safe human use, plus intriguing data suggest that it may possess anti-aging properties, so those with excess blood glucose may consider taking it even if they are not diagnosed as diabetic.57 Some of the side benefits of metformin include weight loss, which itself is a proven heart attack risk reducer. The dose of metformin varies considerably. The starting dose may be as low as **250-500** mg once a day with a meal. If hypoglycemia (low blood sugar) does not manifest, the dose of metformin may be increased to **500-850** mg taken before the two largest meals of the day, all under the supervision of your physician, of course. One side effect of metformin is that it can cause homocysteine levels to elevate.58 The next section discusses safe methods to suppress excess homocysteine. Those with impaired kidney function should not take metformin.



Another drug that lowers glucose levels is **acarbose**, which reduces the absorption of ingested carbo-hydrates by inhibiting the *alpha-glucosidase* enzyme in the small intestine. A typical dose is 50 mg of acarbose taken before each meal (three times a day). Some people experience intestinal side effects, but otherwise, acarbose is highly efficacious in reducing blood glucose levels and reducing several cardiac risk markers in the blood.59-61

Nutrient options:

- 1. Several nutrients block carbohydrate-digesting enzymes in the digestive tract in a similar manner to the drug acarbose. Dietary supplements such as Salacia oblonga or Salacia reticulata extracts inhibit the alpha-glucosidase enzyme and thus decrease the breakdown of simple carbohydrates in the intestine, resulting in a slower and lower rise in blood glucose throughout the day, especially after meals.62,63 Alpha-glucosidase inhibitors (described above) interfere with the breakdown of simple carbohydrates into glucose. Alpha-amylase inhibitors, on the other hand, interfere with the breakdown of large carbohydrate molecules like starch into linked glucose polymers. These simple sugars are then broken down to glucose by the alpha-glucosidase enzyme. The best documented alpha-amylase inhibitor consists of an extract from the white kidney bean (Phaseolus vulgaris). In a placebo-controlled study, those taking standardized white kidney bean extract lost 3.8 pounds over a 30-day period. More importantly, they lost 1.5 inches of abdominal fat and their triglycerides plummeted 26 points (milligrams per deciliter).64 There would appear to be an even greater benefit in combating excess blood glucose by taking both an alpha-glucosidase and an alpha-amylase inhibitor. Such combinations will soon be available in dietary supplement form.
- 2. The ingestion of soluble fiber(s) such as **oat beta-glucan**,17-19 **psyllium**,20 **guar gum**,21,22 **pectin**,23,24 and/or **glucomannan**25 can result in significant reductions in fasting **glucose** and post-meal **insulin** release. These fibers also help reduce LDL and total cholesterol. The most common way of using these fibers is to mix them in eight ounces of water and drink them before heavy meals. These fibers can also be taken in capsule form. Start off with relatively modest doses and slowly work up to higher amounts to enable your digestive tract to get used to this higher fiber intake. Depending on the type of soluble fiber you choose, taking **two** to **eight grams** (2,000-8,000 mg) before each meal is a reasonable target to attain.
- 3. **Irvingia** extract, taken in the dose of **150** mg twice a day is associated with beneficial changes in fasting glucose in subjects losing weight over a 10-week period.29-32,65-68
- 4. The mineral **chromium** can improve insulin sensitivity and help lower fasting **glucose.**69-73 The suggested daily dose of elemental chromium is **700-1,000** mcg, preferably in the form of **chromium polynicotinate**, a highly bioavailable chromium that allows for enhanced absorption and utilization of this critical mineral. Take antioxidants such as green tea extract, curcumin, or grape seed with chromium to mitigate chromium's potential free radical-generating effects. Make sure your daily supplement program also includes at least **1,000** mcg of **biotin** to further help maintain glucose control. Biotin enhances insulin sensitivity and increases the activity of glucokinase, the enzyme responsible for the first step in the utilization of glucose by the liver.74-76
- 5. The amino acid **L-carnitine** lowers blood glucose and a measurement of long-term glucose control called *hemoglobin A1C.*77,78 Carnitine does this by increasing insulin sensitivity and glucose storage, while helping to optimize fat and

carbohydrate metabolism. The suggested dose is 1,500-2,000 mg of the more bioavailable acetyl-L-carnitine.

- 6. **Coenzyme Q10** (CoQ10) improves blood sugar control while helping to protect against LDL oxidation. When given to type 2 diabetics, CoQ10 improves glycemic control as measured by lower *hemoglobin A1C*.79,80
- 7. Magnesium deficiency is widespread. Supplementation with magnesium has been shown to reduce fasting glucose and hemo-globin A1C in type 2 diabetics who are magnesium-deficient by improving insulin sensitivity.81 The suggested dose of elemental magnesium is 500 mg a day (and higher for some individuals). Magnesium replenishment can also reduce C-reactive protein.82
- 8. **Cinnamon** contains unique polyphenols that enhance insulin sensitivity and facilitate cellular glucose uptake with subsequent reduction in fasting blood glucose levels. Cinsulin® is a standardized water extract of cinnamon that has demonstrated the most significant glucose control effect in clinical studies.83,84 Cinsulin® has also been shown to reduce triglycerides, total cholesterol, and LDL.83,85-87 The daily dose of Cinsulin® is **175** mg taken before each meal (three times a day).
- 9. Coffee berry contains well-studied phytochemicals such as chlorogenic acid and caffeic acid, which are the two primary nutrients in the coffee berry that benefit individuals with high blood sugar. Glucose-6-phosphatase is an enzyme that promotes the release of stored glucose (glycogen) from the liver. It is often overactive in people with high blood sugar.88 Reducing the activity of the glucose-6-phosphatase enzyme leads to reduced blood sugar levels. Chlorogenic acid has been shown to inhibit the glucose-6-phosphatase enzyme resulting in reduced glucose production.89 Chlorogenic acid also has an antagonistic effect on glucose transport, decreasing the intestinal absorption rate of glucose.90 Caffeic acid increases glucose uptake into cells, helping remove it from the bloodstream.91 The suggested daily dose of standardized coffee berry extract is 100-200 mg.

Dietary options:

- 1. Consume a **very low-calorie diet** (often less than 1,400 calories a day). Most people cannot adhere to a very low-calorie diet.33
- 2. Consume a **Mediterranean diet,** with lots of fresh fruits and vegetables, fish and soy as protein sources, and omega-3 and monounsaturated fats (olive oil), while avoiding saturated fats, refined carbohydrates, cholesterol-laden foods, excess omega-6 fats, and most animal products. An increasing percentage of Americans are adopting this kind of diet.34-37
- 3. Avoid sugary fruit juices (almost all fruit juices contain too many sugars) and beverages spiked with fructose, sucrose, and/or high-fructose corn syrup. Consume a low-glycemic index and low-glycemic load diet.

Hormone options: As humans age, they experience a reduction in insulin sensitivity. This enables excess glucose to accumulate in the blood instead of being efficiently absorbed into energy-producing cells such as muscle. Normal aging is also accompanied by a sharp decline in **hormones** that are involved in maintaining insulin sensitivity and hepatic glucose control. Restoring dehydroepiandrosterone (**DHEA**) levels to youthful ranges may help enhance insulin sensitivity and glucose metabolism in the liver.92-95 For men, restoring youthful levels of testosterone has been shown to be particularly beneficial in facilitating glucose control.96 Blood tests can assess your hormonal status so that you can replenish DHEA (and testosterone) to more youthful ranges. Men with pre-existing prostate cancer should avoid testosterone until their cancer is cured and women with certain types of breast cancer are advised to avoid DHEA until their cancer is cured.

HEART ATTACK RISK FACTOR #5: Excess Homocysteine

OPTIMAL BLOOD LEVEL:

Under 7-8 mcmol/L of homocysteine

Homocysteine is a breakdown product of an amino acid (methionine) most commonly found in meats. Those who consume high-meat diets often have higher homocysteine levels. Excess homocysteine also occurs in response to **remethylation** deficits and a deficiency of an enzyme called **cystathionine b-synthase.**

Excess **homocysteine** can both <u>initiate</u> **atherosclerosis** and <u>facilitate</u> its progression.97-99 Some poorly designed studies over the past four years have caused the medical establishment to ignore the atherogenic dangers of excess homocysteine. The problem with these studies is that they used varying doses of B vitamins to induce modest reductions in blood homocysteine levels. When there were no reductions in heart attack incidences, doctors claimed there was no benefit to homocysteine reduction. These studies also failed to *individualize* programs to provide different forms of nutrients to study subjects to ensure

maximum homocysteine reduction. For instance, if your homocysteine level is **16**, and you take a multivitamin preparation that reduces it to **13**, you are unlikely to see a vascular disease risk reduction. If on the other hand you aggressively slash your homocysteine down to below **8**, your risks for a wide range of disorders (including heart attack) may be significantly reduced.

Drug options: Elevated homocysteine blood levels can usually be brought into safer ranges by taking **folic acid**, **vitamin B12**, **trimethylglycine (TMG)**, and **vitamin B6** dietary supplements. Reducing one's intake of methionine-rich foods (such as meats) also assists in reducing homocysteine. There are individuals, however, who suffer from remethylation deficits and/or cystathionine b-synthase deficiencies. In these cases where homocysteine levels remain stubbornly high despite aggressive use of supplements, an expensive prescription drug called **Cerefolin®** is available. This drug contains 5,200 mcg of a special form of folic acid called *L-methylfolate* plus very small amounts of vitamins B12 and B6. The reason this drug is called Cerefolin® is because excess homocysteine is known to damage the brain, ergo the name "Cere"folin to imply "cerebral" folic acid. Due to its high cost, Cerefolin® is recommended only when natural approaches fail.

Nutrient options:

1. To facilitate the **remethylation** of homocysteine into safer compounds such as SAMe (S-adenosyl-methionine), the following nutrients should be taken in the following doses each day:

Folic acid: 800-3,200 mcg100-102 Vitamin B12: 500-2,000 mcg103,104

Trimethylglycine (TMG): 500-8,000 mg₁₀₅₋₁₀₇ Multivitamin with B complex and zinc₁₀₈

(High-dose vitamin C has also been reported to help lower homocysteine).109

2. To facilitate the **cystathionine b-synthase** enzyme that converts homocysteine into beneficial cysteine and glutathione (via the *trans-sulfuration* pathway), increased doses of vitamin B6 are often needed. The high dose of conventional vitamin B6 (pyridoxine HCl) needed to lower homocysteine has raised concerns among some doctors. Fortunately, a form of vitamin B6 called **pyridoxamine** provides the body with the most biologically active form of vitamin B6 in a safe dose range.₁₁₀ To reduce elevated homocysteine, **100-250** mg a day of **pyridoxamine** should be used.

Dietary options:

- 1. Consume a vegan diet devoid of meat, with protein obtained primarily from plant sources (nuts, legumes, and soy).
- 2. Consume a **Mediterranean diet**, with lots of fresh fruits and vegetables, fish and soy as protein sources, and omega-3 and monounsaturated fats (olive oil), while minimizing meats like beef, pork, chicken, and turkey.34-37

REPORT

How to Circumvent 17 Independent Heart Attack Risk Factors

By William Faloon

HEART ATTACK RISK FACTOR #6: Excess C-Reactive Protein

OPTIMAL BLOOD LEVEL:

Under 0.55 mg/L of C-reactive protein in men Under 1.50 mg/L of C-reactive protein in women

Chronically elevated **C-reactive protein** blood levels indicate you are suffering from a continuous systemic **inflammatory** state. Chronic inflammation damages every cell in the body. The chronic inflammation that occurs in the vascular wall is a significant cause of atherosclerosis and subsequent heart attack and stroke.111,112



C-reactive protein is produced in many cells throughout the body. The C-reactive protein that concerns us from a vascular risk standpoint is what is produced by fat cells (adipocytes) and the liver in response to excess interleukin-6 released by abdominal fat that is then dumped directly into the liver.

Drug options: Statin drugs such as **Lipitor**®,113 **simvastatin**,112 **pravastatin**,114 and **Crestor**®115 lower C-reactive protein, as do **aspirin**116,117 and **ibuprofen**.118 In order to significantly reduce C-reactive protein, it sometimes requires daily doses of these drugs that are higher than what many people can safely tolerate. A more pragmatic solution to reduce C-reactive protein is to use natural approaches described below, and take a smaller dose of drugs or no drugs at all. (Note: Low-dose aspirin [81 mg/day] should be taken by virtually anyone seeking to reduce their heart attack risk.)119

Nutrient options: The following nutrients have been shown to either directly reduce **C-reactive protein** or indirectly suppress factors that promote chronic inflammatory reactions in the body:

- 1. Irvingia extract in the dose of 150 mg twice a day.29-32
- 2. Vitamin C in the dose of 1,000 mg a day (and preferably higher).120
- 3. Curcumin in the form of enhanced bioavailable BCM-95® curcumin in the dose of 400 mg taken twice a day.118
- 4. Luteolin (a flavonoid) in the dose of 8-16 mg a day.121-124
- 5. Vitamin K in the dose of 1,000 mcg of K1; 1,000 mcg of MK-4; and 100 mcg of MK-7 each day.125,126
- 6. **Fish oil** in the dose of **1,400** mg of EPA and **1,000** mg of DHA each day, preferably with sesame lignans to enhance the anti-inflammatory effect.₁₂₇₋₁₃₀
- 7. Borage oil supplying 285-1,140 mg of GLA each day.131,132
- 8. Theaflavins extracted from black tea in the dose of 375 mg a day.133-137
- 9. Coenzyme Q10, preferably in the ubiquinol form, in the daily dose of 100-200 mg.138,139
- 10. Vitamin D3 in the dose of 1,000-6,000 IU a day (and higher for some people).140-142

Nutrient-Dietary options: In response to the after-meal surge of ingested sugars and fats into the bloodstream, there are proinflammatory bursts of oxidative stress. The ingestion of soluble fiber(s) such as **oat beta-glucan,**17-19 **psyllium,**20 **guar gum,**21,22 **pectin**23, 24and/or **glucomannan**25 before a meal can slow down the absorption of sugars and fats and reduce the proinflammatory response. These same fibers also reduce LDL, total cholesterol, and glucose.143-146 The most common way of using these fibers is to mix them in eight ounces of water and drink them before most meals. These fibers can also be taken in capsule form. Start off with relatively modest doses and slowly work up to higher amounts to enable your digestive tract to get used to this higher fiber intake. Depending on the type of soluble fiber you choose, taking **two** to **eight grams** (2,000-8,000 mg) before each meal is a reasonable target to attain. Studies document significant reductions in **C-reactive protein** in response to higher fiber ingestion.147,148

Dietary options:

- 1. Lose weight, especially in the abdominal area. Overweight and obese individuals often have significantly higher C-reactive protein levels than lean people.120
- 2. Avoid consuming excess saturated fat and high-glycemic load foods.

- 3. Consume a very low-calorie diet (often less than 1,400 calories a day). Most people cannot adhere to a very low-calorie diet.33
- 4. Consume a Mediterranean diet, with lots of fresh fruits and vegetables, fish and soy as protein sources, omega-3 and monounsaturated fats (olive oil), while avoiding saturated fats, refined carbohydrates, cholesterol-laden foods, excess omega-6 fats, and most animal products. An increasing percentage of Americans are adopting this kind of diet.34-37
- 5. Inclusion of specific **cholesterol-lowering foods** in one's diet can markedly lower LDL, total cholesterol, <u>and</u> **C-reactive protein** levels. Cholesterol-lowering foods with documented proven efficacy include almonds,38 soy protein,38 fiber,19,38 and plant sterols.38
- Avoid foods cooked at high temperature (more than 250 degrees Fahrenheit). Cooking foods at high temperatures results
 in sugars and certain oxidized fats reacting with proteins to form glycotoxins in the food.₁₄₉ Consuming foods high in
 glycotoxins can induce a low-grade chronic state of inflammation.₁₅₀

Hormone options: As humans age, they often encounter a progressive *increase* in systemic inflammation that manifests in the blood as elevated **C-reactive protein.** Normal aging is also accompanied by a severe hormone imbalance. In **men**, <u>low</u> levels of **testosterone** and/or **DHEA** (and <u>excess</u> **estrogen**) are associated with persistent elevations of C-reactive protein.151-153 DHEA deficiencies in women can contribute to chronic inflammatory conditions.154-156 Restoring **DHEA** to youthful ranges may help reduce chronic inflammatory conditions in either sex.



For men, restoring youthful levels of **testosterone** and suppressing excess levels of **estrogen** may be particularly beneficial in combating chronic inflam-matory reactions. Men with pre-existing prostate cancer should avoid testosterone until their cancer is cured and women with certain types of breast cancer are advised to avoid DHEA until their cancer is cured.

Lifestyle modification: People with destructive gum disease almost double their risk of heart attack.157 Studies indicate that *C-reactive protein* levels decline dramatically when periodontal disease is effectively treated.158

HEART ATTACK RISK FACTOR #7: Insufficient Vitamin D

OPTIMAL BLOOD LEVEL:

Over 31 ng/mL of 25-hydroxyvitamin D (Some studies suggest the optimal range is between 50 ng/mL and 65 ng/mL)

Vitamin D has long been known to protect the **bones** and in recent years to lower the risk of many forms of **cancer**. Findings released last year show that men with low vitamin D levels suffer more than twice as many heart attacks.159

Vitamin D may protect against heart disease via several different mechanisms, including reducing chronic inflammatory reactions that contribute to coronary atherosclerosis. 160

Drug options: Potent forms of vitamin D (such **as calcitriol**) are sold as prescription drugs and may benefit individuals with certain kidney disorders.

For most people, however, there is no reason to consider these drugs when super low-cost vitamin D3 supplements are widely available.

Nutrient options: Vitamin D3 can be taken in supplemental form at the minimum dose of **1,000** IU a day, though most people could benefit greatly from higher doses in the range of **6,000** IU each day. The amount of supplemental vitamin D3 one needs is dependent on their body weight (large people need lots more supplemental vitamin D3) and sunlight exposure. When it comes to vitamin D3, it is not the amount ingested that is most important. What matters most is the achieved blood level of a vitamin D metabolite called **25-hydroxyvitamin D**. Conventional medicine does not diagnose vitamin D <u>deficiency</u> until levels drop below **12** ng/mL, yet experts now state that **25-hydroxyvitamin D** levels below **32** ng/mL represent a vitamin D <u>insufficiency</u> that increases one's risk of contracting age-related disease.161,162

Dietary options: While vitamin D is present in healthy foods like fish, one would not want to try to obtain enough vitamin D via their diet as they are unlikely to obtain optimal levels.

Lifestyle options: Vitamin D is synthesized when the skin is exposed to sunlight. Intentional sunlight exposure is not recommended because of increased risks of basal cell, squamous cell, and melanoma skin cancers. Also, the skin of older people often does not efficiently synthesize enough vitamin D.163

HEART ATTACK RISK FACTOR #8: Insufficient Vitamin K

OPTIMAL BLOOD LEVEL:

Vitamin K blood tests assess levels of vitamin K to maintain healthy coagulation, but at this time are not used to identify optimal levels to reduce heart attack risk. Fortunately, there are also considerable data to substantiate that the proper vitamin K supplements correct insufficient vitamin K.164-169

Vitamin K is essential for regulating proteins in the body that direct calcium to the bones and keep it out of the arterial wall. <u>Low vitamin K</u> status predisposes aging humans to arterial calcification, 170-173 chronic inflam-mation, 125, 126 and sharply higher heart attack risks. 174

While most people have enough vitamin K in their blood to ensure healthy blood coagulation, many suffer from <u>insufficient</u> vitamin K to protect against arterial calcification and osteoporosis.₁₇₅₋₁₇₈

Drug options: Vitamin K1 (phytonadione) is sold as a prescription drug, primarily to reverse the effects of a Coumadin® (warfarin) overdose.₁₇₉ Low-cost vitamin K2 supplements are more effective for cardiovascular and bone health benefits in part because they can supply longer-acting forms of vitamin K.

Nutrient options: Vitamin K is sold as a dietary supplement as vitamin **K1**, vitamin **K2** menaquinone-4 (**MK-4**), or vitamin **K2** menaquinone-7 (**MK-7**). The **MK-7** form has generated the most recent excitement because it achieves higher blood levels over a sustained 24-hour period. There is also strong supporting evidence to substantiate the vascular-protective effects of K1 and MK-4. Based on the totality of scientific data, an ideal daily vitamin K intake would consist of:

1,000 mcg of K1

1,000 mcg of MK-4

100 mcg of MK-7

Dietary options: Vitamin K is found in two dietary forms: vitamin K1, which occurs in leafy green vegetables; and vitamin K2, which exists in organ meats, egg yolks, dairy products, and particularly in fermented products such as cheese and curd. While some ingested K1 is converted to K2 in the body, the most significant arterial benefits occur when vitamin K2 itself is supplemented.₁₇₄ The absorption of K2 into the bloodstream is relatively efficient, whereas relatively little K1 is absorbed from plant foods.₁₈₀ The kinds of foods rich in K2 in the Western world (organ meats, eggs, and dairy) should not be eaten in excess. Japanese who eat large quantities of a fermented soybean food called natto have lower rates of heart disease and osteoporosis._{181,182} Natto is naturally rich in vitamin K2, but most people in Western worlds find it unpalatable.



HEART ATTACK RISK FACTOR #9: Elevated Triglycerides

OPTIMAL FASTING BLOOD LEVEL:

Under 80 mg/dL of triglycerides

OPTIMAL FASTING BLOOD LEVEL FOR INDIVIDUALS WITH PRE-EXISTING CARDIOVASCULAR DISEASE:

Under 60 mg/dL of triglycerides

OPTIMAL NON-FASTING BLOOD LEVEL:

Under 116 mg/dL of triglycerides

Triglycerides are the form in which most fat exists within the body. Triglycerides in the blood are derived from fats eaten in foods or are made in the body from other sources like carbohydrates. Calories ingested in a meal that are not used immediately by tissues are converted to triglycerides and transported to fat cells to be stored. Triglycerides are also present in the blood.

Triglycerides can accumulate on the walls of arteries and contribute to the buildup of atherosclerotic plaque. Elevated triglycerides increase risk of stroke and heart attack.183 Elevated blood triglycerides are involved in the deadly metabolic *syndrome* that predisposes individuals to type 2 diabetes and its related vascular complications.184

Triglycerides are the major constituent of belly fat. Excess blood **triglycerides** induce an accumulation of undesirable body fat (especially in the visceral abdominal region). Abdominal obesity is a major risk factor for heart attack, stroke, dementia, and a host of chronic inflammatory diseases.185-187

Conventional medicine says that triglyceride levels up to **149** mg/dL are safe, but *Life Extension* has long maintained that optimal fasting triglycerides are under 100 mg/dL of blood. Now, new evidence suggests that optimal fasting triglyceride levels are even *lower*.

Findings published over the past two years indicate that higher *non-fasting* triglyceride levels significantly increase heart attack and ischemic stroke risk. One study showed that compared to women with non-fasting triglyceride levels less than or equal to **104 mg/dL**, women with a non-fasting triglyceride level of **105-170 mg/dL** had **48% greater incident cardiovascular disease**, and women with a non-fasting triglyceride level of greater than or equal to 171 mg/dL had 94% **greater incident cardiovascular disease**. These results were corrected for baseline differences in age, blood pressure, smoking, and use of hormone therapy.188



Another study found that the 10-year risk of ischemic stroke in men aged 55 years or older with non-fasting triglyceride levels of 443 mg/dL or greater was **about five-fold higher** than in men younger than 55 years with non-fasting triglyceride levels of less than **89 mg/dL**.189 Still another study found heart attack risk was **46% higher** in women and **18% higher** in men for each **88.5** mg/dL increase in non-fasting triglyceride levels after adjustment for age.190

What do these new data mean? In response to eating a meal containing fat or high-glycemic index simple carbohydrates, blood triglyceride levels will increase. Those with healthy metabolic function should rapidly convert these dietary-induced triglycerides into energy or fat storage if needed.

As we age, our ability to healthily metabolize dietary fats and sugars diminishes, resulting in our bloodstream being chronically overloaded with triglycerides that contribute to the development of type 2 diabetes, metabolic syndrome, and obesity. By overconsuming too many of the wrong kinds of calories, many of those following Western dietary patterns are in a state of postprandial (after-meal) hypertriglyceridemia (too many triglycerides in the blood) for most of the day.

What makes the new findings about non-fasting triglycerides so shocking is that it does not require particularly high triglyceride blood levels to substantially increase vascular disease risk. In fact, most doctors consider these kinds of triglyceride readings to be "normal." It is also completely "normal" for aging people to suffer heart attacks and strokes, as these conditions remain the leading causes of death and disability.

A *fasting* blood draw is done 12 hours after eating. A *non-fasting* blood draw may be done 2-8 hours after one eats a typical meal. If *fasting* triglycerides are over 99 mg/dL, there is a good chance your *non-fasting* triglycerides are higher than they should be. We are therefore reducing our recommendation for <u>optimal</u> *fasting* triglyceride level to under 80 mg/dL of blood. We know that achieving this lower level will be challenging to certain individuals, especially those suffering from obesity, type 2 diabetes, and/or metabolic syndrome. Fortunately, there is an arsenal of nutrients and drugs at your disposal that can dramatically slash triglyceride blood levels.

Drug options: The two most effective triglyceride-lowering **prescription drugs** are **Niaspan**®,46 which is extended-release niacin, and **Lovaza**®, which is highly concentrated fish oil.191 The triglyceride-lowering benefits of these drugs can easily be duplicated with low-cost dietary supplements.

Those with stubbornly high triglyceride levels may consider the prescription drug **metformin** in the starting dose of **250 mg** twice a day and moving up to **850 mg** two to three times a day as long as fasting glucose levels do not drop below **72-74** mg/dL of blood. Metformin reduces triglycerides along with glucose.₁₉₂

The prescription drug **orlistat** (**Xenical®** or its over-the-counter version **Alli** Meduces dietary fat absorption by 30% and will drastically reduce triglyceride levels when taken in the dose of 120 mg before each meal (three times a day).193 The gastrointestinal side effects of these kinds of lipase-inhibitor drugs cause us to recommend them for only a 60-day initiation period, with the objective of using them to motivate the user to <u>reduce</u> dietary fat consumption over a long- term basis (even after they discontinue the drug).

The *alpha-glucosidase inhibitor* drug **acarbose** blocks a carbohydrate-degrading enzyme and can reduce triglyceride levels when taken in the dose of 50 mg three times a day.194 *Alpha-glucosidase inhibitors* are also available as low-cost **dietary supplements** (such as *Salacia oblonga* or *Salacia reticulata* extracts). Like acarbose, they function by <u>decreasing</u> the breakdown of simple carbohydrates in the intestine, resulting in a lower rise in blood glucose throughout the day and a corresponding reduction in triglycerides.195,196

Alpha-<u>amylase</u> inhibitors may be even more effective than alpha-<u>glucosidase</u> inhibitors for reducing triglycerides. The best documented alpha-amylase inhibitor consists of an extract from the white kidney bean (*Phaseolus vulgaris*). In a placebo-controlled study, those taking **445** mg/day of white kidney bean extract lost **3.8** pounds over a 30-day period. More importantly, they lost **1.5** inches of abdominal fat and their triglycerides plummeted **26** points (milligrams per deciliter).197

There would appear to be an even greater benefit in combating excess triglyceride blood levels by taking an *alpha-glucosidase* and an *alpha-amylase inhibitor*. Such combinations will soon be available in **dietary supplement** form. Alternatively, one can be prescribed 50 mg three times a day of the drug *acarbose* and take 445 mg a day of a *white kidney bean extract* supplement.

Nutrient options:

- **Fish oil** <u>supplements</u> are the most efficient way for most people to slash elevated triglycerides.198-202 The dose of the EPA/DHA in fish oil taken should be sufficient to reduce triglycerides to optimal ranges. Those with very high triglycerides often need to take relatively high doses of fish oil supplements to accomplish this. For example, an ideal daily dose of fish oil for most people may consist of 1,400 mg of EPA and 1,000 mg of DHA. Those with very high triglycerides may want to double this dose, to 2,800 mg of EPA and 2,000 mg of DHA. One should have their blood re-tested 30-60 days after initiating fish oil supplementation to ensure they are taking the proper dose.
- Niacin in doses of 2,000-3,000 mg a day will significantly lower triglycerides, along with LDL and total cholesterol.3-8,202 Niacin also boosts beneficial HDL while changing LDL particles to a less atherogenic form.5-9 Niacin can cause a skin "flushing" side effect that can be mitigated by taking niacin with aspirin and a meal. Some people cannot tolerate this flushing effect on a daily basis and choose other options to lower triglycerides.
- Green tea contains catechins (flavonoids) that can decrease postprandial fats (such as triglycerides) up to 30%. Approximately 600-700 mg of green tea catechins are required to achieve this effect, the equivalent of 6-12 servings of brewed tea. Nutritional supplements provide green tea catechins at this dose.203 Green tea's effectiveness in accelerating weight loss may in part relate to its ability to reduce excess accumulation of triglycerides after meals. For green tea to be effective, it should be taken immediately before meals to help block the absorption of fats. Use decaffeinated green tea extract supplements if caffeine bothers you.
- Soy protein (20 grams per day) from tofu, soy milk, soy protein powder, and other sources can lower LDL by 10-20 mg/dL and reduce postprandial fats by 10%.204 We suggest that soy be used as part of a healthy diet in which soy protein is substituted for red meat, a source of unhealthy saturated fat and arachidonic acid (the raw material for proinflammatory series 2 prostaglandins).

Dietary-Lifestyle options: Weight loss can greatly reduce triglycerides and postprandial lipoproteins, particularly when it is achieved using a diet that is low in simple carbohydrates, high in protein, and moderate in monounsaturated fats. Cutting out processed carbohydrates (such as breads, crackers, breakfast cereals, bagels, and pretzels made with refined, processed white flour) alone can yield a **30%** reduction in postprandial lipoproteins.205,206 Increasing your intake of yogurt, cottage cheese, and other low-fat dairy products, raw almonds and walnuts, and fish, chicken, turkey, and other sources of lean protein will also yield substantial reductions in postprandial lipoprotein particles. Weight loss restores the insulin responsiveness lost in metabolic syndrome, which also reduces postprandial lipoproteins.

If you are overweight, cut down on calories to reach your ideal body weight. This includes excess calories from fats, proteins, carbohydrates, and alcohol. Reduce the saturated fat, trans fats, and cholesterol content of your diet. Reduce your intake of alcohol considerably as even small amounts of alcohol can lead to large changes in plasma triglyceride levels. Eat vegetables and non-fat or low-fat dairy products most often. Eat whole fruits rich in fiber, but do not overindulge. Fruit sugar (fructose) can raise triglyceride levels when consumed in excess. For this reason, avoid commercial fruit juices due to their concentrated calorie content and high fructose levels. Get at least 30 minutes of moderate-intensity physical activity on five or more days each week. Substitute monounsaturated and certain polyunsaturated fats—such as those found in olive and canola oil—in place of saturated fats. Avoid high-glycemic load foods. Incorporate fish that is high in omega-3 fatty acids (such as mackerel, lake trout, herring, sardines, tuna, and salmon) in place of red meats high in saturated fat and arachidonic acid (the building block for the proinflammatory series 2 prostaglandins).

REPORT

How to Circumvent 17 Independent Heart Attack Risk Factors

By William Faloon

HEART ATTACK RISK FACTOR #10: Low Blood EPA/DHA

OPTIMAL BLOOD LEVEL:

Commercial EPA/DHA blood tests are expensive and not always readily available. Blood triglyceride levels may be used as a partial surrogate marker to ensure sufficient EPA/DHA intake, along with ingesting the suggested daily amount of EPA/DHA from fish.

Scientists long ago documented that those who ingest lots of **EPA/DHA** from coldwater fish have markedly lower heart attack rates. Controlled clinical studies substantiate a significant reduction in heart attacks in response to fish oil-derived EPA/DHA.207



A study measured levels of **EPA/DHA** in patients' blood and established that <u>low</u> **EPA/DHA** was an *independent* risk factor for heart attack. Compared with age-matched controls, the risk of unstable angina or heart attack in these patients was reduced 62% for every 1.24% <u>increase</u> in whole-blood EPA/DHA.208

Drug options: EPA/DHA prescription drugs are available that can cost **seven times** more than comparable EPA/DHA dietary supplements.

Nutrient options: Fish oil supplements are widely available as dietary supplements. For most people, a daily dose of **1,400** mg of **EPA** and **1,000** mg of **DHA** from fish oil provides optimal dosing. The addition of **sesame lignans** has been shown to improve the efficiency of fish oil in the body via several mechanisms._{129,130,209-211} If you are taking 1,400 mg EPA and **1,000** mg DHA and your triglyceride levels are over **80** mg/dL of blood, then you should increase your fish oil intake until triglyceride levels are reduced below 80 mg/dL.

Dietary options: Some studies show that consuming as few as two coldwater fish meals a week reduces heart attack risk.212 We suggest that omega-3 fatty acids (EPA/DHA) should be part of your everyday program, which can be accomplished by eating mackerel, lake trout, herring, sardines, tuna, sea bass, and salmon (and/or by taking EPA/DHA supplements).

HEART ATTACK RISK FACTORS #11 and #12: Low Testosterone and Excess Estrogen (in Men)

OPTIMAL BLOOD LEVEL:

20-24 pg/mL of Free Testosterone (men only) 20-30 pg/mL of Estradiol (men only)

Aging males can suffer the dual consequence of declining testicular **testosterone** production, while the testosterone they do produce is often excessively converted (aromatized) into **estrogen**.

Numerous studies link low testosterone (and excess estradiol) with increased heart attack and stroke risk.40,213-217 Many of these studies have identified specific mechanisms by which an imbalance of these hormones promotes atherosclerosis and subsequent heart attack/stroke incidence.52,218,219 **Testosterone**, for instance, is intimately involved in the *reverse cholesterol transport* process that involves the *removal* of cholesterol from the arterial wall by HDL. Excess **estrogen** is linked with higher C-reactive protein and a greater propensity for abnormal blood clots to form in arteries, causing a sudden heart attack or stroke.213,220,221

Drug options: To restore testosterone to youthful levels, natural testosterone cream is available as a ready-made prescription drug for around \$225 a month, or a physician can prescribe a compounded natural testosterone cream that costs around \$20 a month. The dose of testosterone prescribed should be based on blood tests showing what baseline free testosterone levels are. To suppress excess estrogen, the aromatase-inhibitor drug **Arimidex**® can be prescribed in the low dose of **0.5** mg to be taken twice a week. Men with pre-existing prostate cancer should avoid testosterone until their cancer is cured.

Nutrient options: For men who suffer low testo-sterone (and sometimes excess estrogen) because they express too much aromatase enzyme, nutrients like specialized plant lignans (30 mg a day and higher of HMR™ Ligna)rand Bioperine®-enhanced absorption chrysin (1,500 mg a day) may be all that is needed.222-224 Zinc (50 mg/day) may also help suppress excess aromatase.225

Dietary-lifestyle options: Abdominal fat has a propensity to produce excess aromatase, which converts testosterone into estrogen in aging men.226-228 Losing belly fat with the help of nutrients like **Irvingia** extract can help restore a more youthful hormone balance.30-32 Restoring testosterone to youthful ranges can also help reduce belly fat mass. Excess alcohol consumption can reduce the ability of the liver to remove excess estrogen.

HEART ATTACK RISK FACTOR #13: Excess Insulin

OPTIMAL BLOOD LEVEL:

Under 5 mcIU/mL of fasting insulin (difficult for aging people to achieve)

Aging people lose their ability to utilize insulin to effectively drive blood glucose into energy-producing cells. As glucose levels rise in the blood, the pancreas compensates by producing more insulin. As "insulin resistance" worsens, even more insulin is secreted in a feeble attempt to restore glucose control.

Excess insulin is associated with greater risks of heart attack, stroke, and many cancers.229-232 Many of the same strategies you read earlier to lower excess **glucose** also lower excess **insulin.**

Drug options: The prescription drug **metformin** helps to improve insulin sensitivity and suppress factors in the body involved in causing excess blood glucose.57,233,234 **Metformin** is available in low-cost generic form and has a long enough history of safe human use for those with excess blood insulin to consider taking it even if they are not diagnosed as diabetic. Some of the side benefits of metformin include weight loss, which itself is a proven heart attack risk reducer.235 The dose of metformin varies considerably. The starting dose may be as low as **250-500** mg once a day with a meal. If hypoglycemia (low blood sugar) does not manifest, the dose of metformin may be increased to **500-850** mg taken before the two largest meals of the day, all under the supervision of your physician, of course. One side effect of metformin is that it can cause homocysteine levels to elevate.58 Those with impaired kidney function should not take metformin.

Another drug that lowers insulin levels is **acarbose**, which reduces the absorption of ingested carbohydrates by inhibiting the *alpha-glucosidase* enzyme in the small intestine. A typical dose is 50 mg of acarbose taken before each meal (three times a day). Some people experience intestinal side effects, but otherwise, acarbose is highly efficacious in reducing blood glucose and subsequent excess insulin release.59-61

Nutrient options:

1. Several nutrients block carbohydrate enzymes in the digestive tract in a similar manner to the drug acarbose. Dietary supplements such as Salacia oblonga or Salacia reticulata extracts inhibit the alpha-glucosidase enzyme and thus decrease the breakdown of simple carbohydrates in the intestine, resulting in a slower and lower rise in blood glucose and insulin throughout the day, especially after meals.62,63 Alpha-glucosidase inhibitors (described above) interfere with the breakdown of simple carbohydrates into glucose. Alpha-amylase inhibitors, on the other hand, interfere with the breakdown of large carbohydrate molecules like starch into linked glucose polymers. These simple sugars are then broken down to glucose by the alpha-glucosidase enzyme. The best documented alpha-amylase inhibitor consists of an extract from the white kidney bean (Phaseolus vulgaris). In a placebo-controlled study, those taking standardized white kidney bean extract lost 3.8 pounds over a 30-day period. More importantly, they lost 1.5 inches of abdominal fat and their triglycerides plummeted 26 points (milligrams per deciliter).64 There would appear to



be an even greater benefit in combating excess blood glucose and insulin by taking both an *alpha-glucosidase* and an *alpha-gmylase* inhibitor. Such combinations will soon be available in dietary supplement form.

2. The ingestion of soluble fiber(s) such as oat beta-glucan, 17-19 psyllium, 20 guar gum, 21,22 pectin, 23,24 and/or glucomannan25 can result in significant reductions in post-meal insulin release. The most common way of using these fibers is to mix them in eight ounces of water and drink them before heavy meals. These fibers can also be taken in capsule form. Start off with relatively modest doses and slowly work up to higher amounts to enable your digestive tract to get used to this higher fiber intake. Depending on the type of soluble fiber you choose, taking two to eight grams (2,000-8,000 mg) before each meal is a reasonable target to attain.

- 3. **Irvingia** extract, taken in the dose of **150** mg twice a day is associated with beneficial changes in fasting **glucose** with weight loss.65-68
- 4. The mineral **chromium** can improve insulin sensitivity and help lower fasting **glucose.**69-73 The suggested daily dose of elemental chromium is **700-1,000** mcg, preferably in the form of **chromium polynicotinate**, a highly bioavailable chromium that allows for enhanced absorption and utilization of this critical mineral. Take antioxidants such as green tea extract, curcumin, or grape seed with chromium to mitigate chromium's potential free radical-generating effects. Make sure your daily supplement program also includes at least **1,000** mcg of **biotin** to further help maintain glucose control. Biotin enhances insulin sensitivity and increases the activity of glucokinase, the enzyme responsible for the first step in the utilization of glucose by the liver.74-76
- 5. The amino acid **L-carnitine** lowers blood glucose and a measurement of long-term glucose control called **hemoglobin A1C.**77,78 Carnitine does this by increasing insulin sensitivity and glucose storage, while helping to optimize fat and carbohydrate metabolism. The suggested dose is **1,500-2,000 mg** of the more bioavailable **acetyl-L-carnitine**.
- 6. Magnesium deficiency is widespread. Supplementation with magnesium has been shown to reduce fasting glucose and hemoglobin A1C in type 2 diabetics who are magnesium-deficient by improving insulin sensitivity.81 The suggested dose of elemental magnesium is 500 mg a day (and higher for some individuals). Magnesium replenishment can also reduce C-reactive protein.82
- 7. **Cinnamon** contains unique polyphenols that enhance insulin sensitivity and facilitate cellular glucose uptake with subsequent reduction in fasting blood glucose levels. Cinsulin® is a standardized water extract of cinnamon that has demonstrated the most significant glucose control effect in clinical studies.83,84 Cinsulin® has also been shown to reduce triglycerides, total cholesterol, and LDL.85-87 The daily dose of Cinsulin® is **175** mg taken before each meal (three times a day).

DIETARY OPTIONS:

- 1. Consume a **very low-calorie diet** (often less than 1,400 calories a day). This is by far the most effective way to dramatically reduce insulin levels. The problem is that few people can adhere to a diet this low in calories.33
- 2. Consume a **Mediterranean diet**, with lots of fresh fruits and vegetables, fish and soy as protein sources, omega-3 and monounsaturated fats (olive oil), while avoiding saturated fats, refined carbohydrates, cholesterol-laden foods, excess omega-6 fats, and most animal products. An increasing percentage of Americans are adopting this kind of diet.34-37
- 3. Avoid sugary fruit juices (almost all fruit juices contain too many sugars) and beverages spiked with fructose, sucrose and/or high-fructose corn syrup. Consume a low-glycemic index and low-glycemic load diet.

Hormone options: As humans age, they experience a reduction in insulin sensitivity. This enables excess glucose to accumulate in the blood instead of being efficiently absorbed into energy-producing cells such as muscle. Normal aging is also accompanied by a sharp decline in **hormones** that are involved in maintaining insulin sensitivity and hepatic glucose control. Restoring **DHEA** to youthful ranges may help enhance insulin sensitivity and glucose metabolism in the liver.92-95 For men, restoring youthful levels of **testosterone** has been shown to be particularly beneficial in facilitating insulin sensitivity.96,236 Blood tests can assess your hormonal status so that you can replenish DHEA (and testosterone) to more youthful ranges. Men with pre-existing prostate cancer should avoid testosterone until their cancer is cured and women with certain types of breast cancer are advised to avoid DHEA until their cancer is cured.

HEART ATTACK RISK FACTOR #14: Nitric Oxide Deficit

Optimal Blood Level: Commercial blood tests are not yet available at affordable prices to assess nitric oxide status. Aging individuals should assume they are developing a nitric oxide deficit in their inner arterial wall (the endothelium) and follow simple steps to protect themselves.

Even when all other risk factors are controlled for, the age-related decline in endothelial **nitric oxide** too often causes accelerated atherosclerosis unless corrective measures are taken.

Nitric oxide is *required* for healthy inner arterial wall (endothelial) function. Nitric oxide enables arteries to expand and contract with youthful elasticity and is vital to maintaining the structural integrity of the endothelium, thus protecting against atherosclerosis. The age-related deficiency in endothelial-derived nitric oxide predisposes maturing humans to today's epidemic of heart attack and stroke.237-239

Drug options: One of the little-known benefits of statin drugs is that they promote endothelial nitric oxide synthesis.²⁴⁰ Our current recommendation is for aging people to take the lowest statin drug dose to achieve desired LDL levels. Some people only require **5-10 mg** of **simvastatin** or **20-40 mg** of **pravastatin** per day. At these modest doses, side effects are rare. Supplemental CoQ10 is needed to protect against statin-drug induced coenzyme Q10 deficiency.^{1,2}

Nutrient options: The classic nutrient to boost **nitric oxide** levels is high-dose **arginine**, an amino acid found in many foods. Arginine is a precursor to the natural synthesis of nitric oxide in the endothelium. The problem is that arginine is rapidly degraded in the body by five different enzymes, thus requiring dosing of arginine every 4-6 hours. Even if one were to take this much arginine, changes that occur in the arteries of aging people cause rapid *depletion* of endothelial nitric oxide. A more effective way of boosting nitric oxide is to protect it from excessive *degradation*. One of the many beneficial vascular effects of **pomegranate** is its ability to <u>increase</u> *endothelial* **nitric oxide** levels.241-243 By virtue of its effect in restoring nitric oxide, **pomegranate** may help combat *endothelial dysfunction*—the leading cause of atherosclerosis. Daily consumption of eight ounces of pure pomegranate juice has been used in human studies that show significant regression of markers of atherosclerotic occlusion.50,244-248 There is concern that the sugar calories in



pomegranate juice could create glucose control issues. There are **standardized pomegranate** supplements that provide the active constituents of eight ounces of pomegranate juice in **400-500** mg capsules. Additional nutrients that can protect precious nitric oxide against degradation include a patented SOD-boosting complex called **GliSODin®** and **standardized cocoa polyphenols.**249,250

Dietary options: Consuming fruits (pomegranate), berries (blueberry, raspberry), and teas (green tea) that contain polyphenols can protect nitric oxide from oxidative degradation.242,251,252

HEART ATTACK RISK FACTOR #15: Excess Fibrinogen

OPTIMAL BLOOD LEVEL:

Less than 300 mg/dL of fibrinogen

Many heart attacks and strokes are caused by a blood clot that obstructs the flow of blood to a portion of the heart or brain. When blood flow is interrupted, cells are deprived of oxygen and die. The build-up of atherosclerotic plaque increases the risk of abnormal blood clotting inside arteries.

Blood clots kill more than 600,000 Americans every year, yet conventional medicine has largely ignored well-documented methods of reducing abnormal blood clot formation.253,254

Low-dose aspirin and certain nutrients (like plant polyphenols) provide partial protection against abnormal blood clots, but the risks associated with excess **fibrinogen** mandate that additional measures be taken to prevent heart attacks and strokes.

Fibrinogen is a component of blood involved in the clotting process. High levels of fibrinogen predispose a person to coronary and cerebral artery disease, even when other known risk factors such as cholesterol are normal.255-258

Drug options: Prescription drugs that lower fibrinogen (like gemfibrozil) have side effects that have precluded their routine use. Statin drugs can indirectly reduce fibrinogen by lowering LDL levels.

Nutrient options: Nutrients that people take to reduce other heart attack risk factors also lower fibrinogen. These include:

- 1. Fish oil in the dose of about 2,000 mg of EPA and 1,250 mg of DHA.259-261
- 2. Vitamin C in the dose of 2,000 mg a day (note that 1,000 mg of vitamin C did not lower fibrinogen in this study).262
- 3. Soy natto extract supplying 2,000 fibrinolytic units of **nattokinase** (NSK-SD™ in the dose **df00-200** mg a day.263
- 4. New Zealand pine bark proanthocyanidins (Enzogenol® in the dose of 240-480 mg a day).264
- 5. Enteric-coated **bromelain** proteolytic enzyme extract (2,400 GDU per gram/5,200 FIP per gram activity) in the dose of one **500** mg capsule two times daily.265,266

Dietary-lifestyle options: Avoid exposure to cold temperatures, as cold increases fibrinogen by 11%.267 Incorporate olive oil into your diet and avoid high-cholesterol foods and saturated fats. Keep homocysteine levels low as excess homocysteine interferes with the natural breakdown of fibrinogen in the body (refer to Heart Attack Risk Factor #5 to review ways of suppressing excess homocysteine).

HEART ATTACK RISK FACTOR #16: Hypertension

Optimal Blood Pressure level:

Systolic blood pressure: Under 115 mmHg Diastolic blood pressure: Under 76 mmHg

This risk factor for heart attack and stroke cannot be detected by a blood test. One's **blood pressure** should be checked regularly by a medical professional. Home blood pressure monitoring devices can also help keep track of blood pressure and assess the efficacy of antihypertensive drugs or natural therapies.

High blood pressure causes hundreds of thousands of Americans to needlessly die each year. Most people will develop hypertension at some point in their life. Since hypertension is not new, and antihypertensive drugs are not extensively promoted to the public, vast numbers of even health-conscious people neglect this critical part of a heart attack prevention program.

Many doctors allow a patient's blood pressure to reach **140/90 mmHg** before prescribing antihypertensive drugs. This can be a lethal mistake. While the standard upper limit for blood pressure has been **120/80 mmHg** for decades, findings from a myriad of published studies reveal that optimal blood pressure ranges are under **115/76 mmHg**.268-271 What this means is that many people are being told by their doctors that their blood pressure is fine, when it really is much too high. Another common error is improperly prescribing antihypertensive drugs that either fail to lower blood pressure enough, or allow gaps at certain times of the day when blood pressure shoots too high.



According to a study published in the *Journal of the American Medical Association*, the risk of cardiovascular disease incrementally increases when blood pressure readings pass **115/75 mmHg.**272 Plain and simple, this means that the vast *majority* of adults living in the Western world are walking around with blood pressure that is dangerously too high!

Drug options: Concern about side effects has kept too many people from using safe antihypertensive medications. The cleanest and most effective anti-hypertensive drugs are the *angiotensin II receptor antagonists*. **Cozaar**® is a popular drug in this class and should be taken in the dose of 25-50 mg two times a day.273 Once-a-day dosing of Cozaar® and many other antihypertensive drugs does not always provide all-day reduction in blood pressure. A once-a-day drug in this class of antihypertensives is called **Benicar**®, which can be taken in the daily dose of 20-40 mg a day.274 Additional antihypertensive medications can be added if blood pressure is not adequately reduced.

Nutrient Options: There are a number of nutrients that can assist in lowering blood pressure and may help mitigate some of the damaging effects that hypertension inflicts. Under no circumstances, however, should anyone assume that taking these nutrients will protect against a heart attack or stroke if their blood pressure is not brought under control, using either antihypertensive drugs and/or dietary and lifestyle modifications. Nutrients that have been shown to reduce blood pressure include:

- 1. C12 casein peptide (whey concentrate-CVH 15™) in the dose df,700 mg once or twice a day as needed.275-277
- 2. **Pomegranate** standardized for the active constituents found in eight ounces of pomegranate juice (usual dose is **400-500** mg each day).278
- 3. **Magnesium** in the dose of 500-1,000 mg each day.265,279,280
- 4. Vitamin C in the dose of 1,000 mg a day (and preferably higher).281-283
- 5. Vitamin D3 in the dose of 1,000-6,000 IU a day (and higher for some people).284,285
- 6. Fish oil in the dose of 1,400 mg of EPA and 1,000 mg of DHA each day.271,286-289
- 7. Coenzyme Q10 preferably in the ubiquinol form, in the daily dose of 100-200 mg.290-292
- 8. Grape seed extract in the dose of 150 mg a day.293,294
- 9. Garlic in the dose of 1,200-1,800 mg a day using Kyolic™ aged garlic extracts
- 10. Adequate dietary or supplemental intake of calcium and potassium.296

Dietary-lifestyle options: Blood pressure can be brought down in a significant number of people if they modify their lifestyle by losing weight, cutting out salt, consuming a healthy diet, and stopping smoking. The Dietary Approaches to Stop Hypertension (DASH) diet is recommended by both mainstream and integrative medical practitioners as a first-line approach to manage hypertension.272,297 The DASH diet is high in fruits, vegetables, and other nutritious foods that are rich in potassium, calcium, and magnesium. People who utilize the DASH diet are encouraged to decrease their saturated fats and replace them with foods high in monounsaturated fats and omega-3 fatty acids, such as those found in fish. Salt restriction is also a major part of the DASH diet—recommendations are that people with hypertension limit their salt intake to less than 2,400 mg (about one teaspoon) a day. Studies have shown



that people who follow the DASH diet can decrease their systolic pressure by 11 points and their diastolic pressure by about six points.298 Obesity puts a person at increased risk of developing hypertension at an early age, as well as developing more severe

hypertension. With weight loss, hypertension can be significantly controlled. In a seven-year study of people who restricted their salt intake and were on a weight-loss program, 80% of the people who stayed on the diet lowered their blood pressure to such a degree that they were able to completely stop their prescription blood pressure medication.²⁹⁹ A lifelong calorie-restriction program will significantly lower blood pressure, but few people can adhere to these kinds of very low-calorie diets.^{300,301}

Hormone options: Sex hormone receptor sites are present in the inner lining of the arterial system (the endothelium). As men and women age, their sex hormones decline as their blood pressure increases. Men should refer to Heart Attack Risk Factors #11 and 12 to review how they can safely restore testosterone levels to youthful ranges. Aging women (without pre-existing hormone-sensitive cancer) should seek to maintain more youthful levels of estrogens and progesterone to help control blood pressure.

REPORT

How to Circumvent 17 Independent Heart Attack Risk Factors

By William Faloon

HEART ATTACK RISK FACTOR #17: Oxidized LDL

Optimal Blood Level: Commercial blood tests are not yet available at affordable prices to measure oxidized LDL. Aging individuals should assume their endogenous antioxidant levels (superoxide dismutase, catalase, and glutathione) are being depleted and that the oxidation of their LDL (low-density lipoprotein) is progressively worsening.



The over-promotion of "statin" drugs has resulted in today's cardiologists focusing on reducing their patient's **LDL** and total **cholesterol** <u>levels</u>. Pharmaceutical company advertising makes it appear as if the only cause of atherosclerosis is excess LDL and cholesterol.

Beginning in **1979**, however, researchers made discoveries indicating that the <u>oxidation</u> of **LDL** results in severe arterial damage. Thousands of studies now reveal how <u>oxidized</u> LDL contributes to the entire atherosclerotic process from start to finish.³⁰²

Drug options: Statin drugs help protect against LDL oxidation; however, by inhibiting coenzyme Q10 synthesis, they deprive the body of one of its most important protectors against LDL oxidation.

Nutrient options: Most *Life Extension* members take nutrients that have been shown to significantly reduce LDL oxidation such as **gamma tocopherol**,303,304 **sesame lignans**,305 and **lycopene**.306,307 A number of studies document the ability of ubiquinol **CoQ10** to protect against **LDL** <u>oxidation</u> better than lycopene, alpha tocopherol, and other lipid-soluble antioxidants.308 Perhaps no other nutrient has demonstrated better *anti-LDL oxidation* effects than **pomegranate**. In a clinical study, human subjects taking pomegranate showed a remarkable **90%** <u>reduction</u> in the LDL basal oxidative state.50 There are **standardized pomegranate** supplements that provide the active constitutents shown to reduce LDL oxidation. The usual dose is **400-500** mg of these **standardized pomegranate** capsules a day. The suggested dose for **ubiquinol** to reduce LDL oxidation is **100-200** mg a day.

Dietary options: The term *postprandial oxidative stress* means the oxidation that occurs after ingesting a meal. The higher the calorie, sugar, and fat content of the meal, the greater the level of post-meal oxidative stress. Reduce calorie content and take antioxidant supplements with each meal. Some people also consume polyphenol-rich beverages such as **green tea, red wine,** or **pomegranate juice** with meals to reduce *postprandial oxidative stress*.50,203,242,309 Beware of the high sugar calories in red wine and pomegranate juice.

Hormone options: The hormones melatonin and DHEA confer significant protection against LDL oxidation. As these hormones decline with normal aging, LDL oxidation increases, as does heart attack and stroke risk. Aging humans can supplement with melatonin doses as low as 300 mcg all the way up to 10-20 mg. Women usually need only modest DHEA dosing (15-25 mg in the morning), whereas men usually need 50 mg of DHEA each morning and sometimes higher. A DHEA blood test enables one to restore their DHEA to the optimal youthful range of 500-640 mcg/dL for men and 250-380 mcg/dL for women. Those with hormone-sensitive cancers are often advised to avoid DHEA.

VIRTUALLY NO ONE SHOULD BE HAVING HEART ATTACKS TODAY!

A question that future medical historians may ask is why so many people kept having heart attacks and strokes when **proven** ways existed to detect and correct the known risk factors.

Based on decades of intensive scientific research, the underlying causes of heart attack and stroke are not a mystery. For reasons that relate to apathy and ignorance, along with drug company propaganda, the majority of aging humans are walking around with a time bomb (coronary atherosclerosis) ticking in their chests. Many are doing nothing to prevent heart attack, while others are making such partial efforts that they are only postponing the inevitable.

I spent an inordinate amount of time assembling the data to write this article because I am shocked that so many dedicated *Life Extension* members are failing to correct for <u>all</u> **17** of these <u>proven</u> vascular disease risk factors. Please remember, if you do

almost everything right, but ignore even <u>one</u> of these 17 risk factors, you subject yourself to the horrific consequences of blockage of critical arteries that carry blood to your heart, brain, and kidneys.

It is my sincere desire to never again hear from a health-conscious person that they have been diagnosed with **coronary artery occlusion.** That's why we have made **comprehensive blood testing** available at ultra-low prices.

With the data presented in this article, you can order low-cost blood tests, find out what your heart attack vulnerabilities are, and take immediate corrective actions. You should also make sure you know your blood pressure and take whatever steps are needed to keep it at 115/75 mmHg or lower (there are exceptions to this, such as those suffering from diabetic and certain kidney disorders).

To order a panel of comprehensive blood tests at the **lowest prices** of the year, call **1-800-208-3444** or log on to www.lef.org/blood. Please order these tests by **June 1, 2009** to save more than **80%** compared with what commercial labs charge.

To view the comprehensive blood test panels available to Foundation members, visit the Blood Test link above.

If you have any questions on the scientific content of this article, please call a Life Extension Health Advisor at 1-800-226-2370.

References

- 1. Proc Natl Acad Sci USA. 1990 Nov;87(22):8931-4.
- 2. Journal of Atheroscler Thromb. 2005;12(2):111-9.
- 3. Zhonghua Yi Xue Za Zhi. 2006 Sep 12;86(34):2399-403.
- 4. JAMA. 2000 Sep 13;284(10):1263-70.
- 5. Am J Cardiol. 2000 Dec 21;86(12A):46L-50L.
- 6. Arch Intern Med. 2000 Apr 24;160(8):1177-84.
- 7. J Am Acad Nurse Pract. 2004 Dec;16(12):526-34.
- 8. J Am Coll Cardiol. 1986 Dec;8(6):1245-55.
- 9. J Ethnopharmacol. 2002 Jan;79(1):81-7.
- 10. J Nutr Sci Vitaminol (Tokyo). 2005 Dec;51(6):413-8.
- 11. Yakugaku Zasshi. 2007 Feb;127(2):385-8.
- 12. Indian J Exp Biol. 2001 Aug;39(8):760-6.
- 13. R&D Laboratory, Arjuna Natural Extracts Ltd PBNO 126 Alwaya Cohin Karala India. Amlamax™ in management of dyslipidemia in humans. 2007.
- 14. R&D Laboratory, Arjuna Natural Extracts Ltd PBNO 126 Alwaya Cohin Karala India. Reduction of the risk of coronary heart disease (CHD) through a multi component targeting, including CRP-levels using Amlamax[™] (AE•205) the standardized dry extract of Emblica officianalis Gaertn. (Indian gooseberry). 2007.
- 15. Br J Nutr. 2007 Jun;97(6):1187-95.
- 16. Yakugaku Zasshi. 2005 Jul;125(7):587-91.
- 17. Am J Ther. 2007 Mar-Apr;14(2):203-12.
- 18. Diabetes Care. 2006 May;29(5):976-81.

- 19. J Nutr. 2003 Mar;133(3):808-13.
- 20. Am J Clin Nutr. 1999 Oct;70(4):466-73.
- 21. J Nutr. 1989 Dec;119(12):1925-31.
- 22. Br J Nutr. 1996 Jul;76(1):63-73.
- 23. Am J Cardiol. 1997 Jan 1;79(1):34-7.
- 24. Am J Clin Nutr. 1997 Nov;66(5):1183-7.
- 25. Am J Clin Nutr. 2008 Oct;88(4):1167-75.
- 26. Arch Intern Med. 2003 Jun 23;163(12):1448-53.
- 27. J Nutr. 2003 Oct;133(10):3298S-302S.
- 28. J Nutr. 2003 Oct;133(10):3293S-7S.
- 29. Nutrition J. 2008 (submitted).(References continued on page 80)
- 30. Lipids Health Dis. 2005 May 25;4:12.
- 31. J Food Technol. 2005;3(4): 472-4.
- 32. Lipids Health Dis. 2008 Nov 13;7:44.
- 33. Atherosclerosis. 2009 Mar;203(1):206-13.
- 34. Nutr Rev. 2006 Feb;64(2 Pt 2):S27-S47.
- 35. J Am Coll Nutr. 2007 Oct;26(5):434-44.
- 36. Lipids Health Dis. 2007 Sep 19;6:22.
- 37. J Am Coll Cardiol. 2004 Jul 7;44(1):152-8.
- 38. JAMA. 2003 Jul 23;290(4):502-10.
- 39. Aging Male. 2002 Jun;5(2):98-102.
- 40. Int J Cardiol. 2005 May 11;101(1):105-10.
- 41. J Atheroscler Thromb. 1996;3(1):45-51.
- 42. J Clin Endocrinol Metab. 2000 Jul;85(7):2370-7.
- 43. J Steroid Biochem Mol Biol. 2005 Apr;94(5):461-7.
- 44. J Steroid Biochem Mol Biol. 1994 Aug;50(3-4):205-12.
- 45. Science. 1984 Sep 7;225(4666):1032-4.
- 46. www.niaspan.com/.
- 47. Coron Artery Dis. 1996 Apr;7(4):321-6.

- 48. Indian J Physiol Pharmacol. 2001 Jan;45(1):71-9.
- 49. Clin Biochem. 2006 Aug;39(8):821-5.
- 50. Clin Nutr. 2004 Jun;23(3):423-33.
- 51. Mol Cell Biol. 2004 Jun;24(12):5209-22.
- 52. Rom J Intern Med. 2007;45(1):17-27.
- 53. Am J Physiol Endocrinol Metab. 2003 Jun;284(6):E1112-8.
- 54. Biochem Biophys Res Commun. 2002 Sep 6;296(5):1051-7.
- 55. Diabetes Care. 1999 Jan;22(1):45-9.
- 56. Proc Natl Acad Sci USA. 1992 Dec 1;89(23):11533-7.
- 57. Drugs. 1999;58(Suppl 1):71-3.
- 58. Scand J Clin Lab Invest. 1997 Oct;57(6):521-7.
- 59. J Atheroscler Thromb. 2008 Jun;15(3):154-9.
- 60. Stroke. 2004 May;35(5):1073-8.
- 61. Endocr Pract. 2006 Jan-Feb;12(Suppl 1):56-9.
- 62. Nutrition. 2005 Jul-Aug;21(7-8):848-54.
- 63. J Am Diet Assoc. 2005 Jan;105(1):65-71.
- 64. Altern Med Rev. 2004 Mar;9(1):63-9.
- 65. Ann Nutr Metab. 1993;37(1):14-23.
- 66. West Afr J Med. 1990 Apr-Jun;9(2):108-15.
- 67. Afr J Trad CAM. 2006;3:74-7.
- 68. Afr J Trad CAM. 2006;3(4):94-101.
- 69. Diabetes Res Clin Pract. 1995 Jun;28(3):179-84.
- 70. Saudi Med J. 2000 Jan;21(1):45-50.
- 71. Ned Tijdschr Geneeskd. 2004 Jan 31;148(5):217-20.
- 72. Altern Med Rev. 2002 Jun;7(3):218-35.
- 73. Diabetes. 1997 Nov;46(11):1786-91.
- 74. J Nutr Sci Vitaminol (Tokyo). 1996 Dec;42(6):517-26.
- 75. Med Hypotheses. 1999 May;52(5):401-6.
- 76. Nippon Rinsho. 1999 Oct;57(10):2261-9.

- 77. J Am Coll Nutr. 1999 Feb;18(1):77-82.
- 78. Eur J Clin Nutr. 2005 Apr;59(4):592-6.
- 79. Eur J Clin Nutr. 2002 Nov;56(11):1137-42.
- 80. Therosclerosis. 2003 May;168(1):169-79.
- 81. Diabetes Care. 2003 Apr;26(4):1147-52.
- 82. Eur J Nutr. 2007 Jun;46(4):230-7.
- 83. J Agric Food Chem. 2000;48:849-52.
- 84. Horm Metab Res. 2004 Feb;36(2):119-25.
- 85. Diabetes Care. 2003 (26):3215-8.
- 86. Diabetes Obes Metab. 2007 Nov;9(6):895-901.
- 87. Proc Nutr Soc. 2008 Feb;67(1):48-53.
- 88. Diabetes. 2005 Jul;54(7):1942-8.
- 89. J Med Chem. 1997 Jan 17;40(2):137-45.
- 90. Am J Clin Nutr. 2003 Oct;78(4):728-33.
- 91. Naunyn Schmiedebergs Arch Pharmacol. 2000 Aug;362(2):122-7.
- 92. Diabetes. 2005 Mar;54(3):765-9.
- 93. Clin Endocrinol (Oxf). 2006 Jan;64(1):46-52.
- 94. J Endocrinol. 1996 Sep;15(Suppl):S43-50.
- 95. Endocr J. 2005 Dec;52(6):727-33.
- 96. Clin Endocrinol (Oxf). 2005 Sep;63(3):239-50.
- 97. Atherosclerosis. 2005 Jul;181(1):159-65.
- 98. Med Clin (Barc). 2003 Nov 1;121(15):561-4.
- 99. Int J Cardiol. 1997 Aug 8;60(3):295-300.
- 100. Clin Sci (Lond). 2005 May;108(5):449-56.
- 101. Lancet. 2000 Feb 12;355(9203):517-22.
- 102. J Nephrol. 2003 Jul-Aug;16(4):522-34.
- 103. Metabolism. 2002 Jul;51(7):881-6.
- 104. Asia Pac J Clin Nutr. 2007 16(1):103-9.
- 105. Mol Genet Metab. 2006 Jul;88(3):201-7.

- 106. Arterioscler Thromb Vasc Biol. 2005 Feb;25(2):379-85.
- 107. J Nutr. 2007 Apr;137(4):1124.
- 108. J Nutr. 2000 Dec;130(12):3090-6.
- 109. Circulation. 1999 Mar 9;99(9):1156-60.
- 110. J Biol Chem. 2000 Jul 14;275(28):21177-84.
- 111. Arch Intern Med. 2004 Sep 13;164(16):1781-7.
- 112. Mayo Clin Proc. 2008 Mar;83(3):333-42.
- 113. Int J Cardiol. 2009 Feb 11.
- 114. Am Heart J. 2003 Feb;145(2):e8.
- 115. N Engl J Med. 2008 Nov 20;359(21):2195-207.
- 116. N Engl J Med. 1997 Apr 3;336(14):973-9.
- 117. Circulation. 1999 Aug 24;100(8):793-8.
- 118. Immunopharmacol Immunotoxicol. 2003 May;25(2):213-24.
- 119. JAMA. 2007 May 9;297(18):2018-24.
- 120. Free Radic Biol Med. 2009 Jan 1;46(1):70-7.
- 121. J Nutr. 2006 Jun;136(6):1517-21.
- 122. Biochem Pharmacol. 2005 Jan 15;69(2):241-8.
- 123. Biol Pharm Bull. 2002 Sep;25(9):1197-202.
- 124. J Pharmacol Exp Ther. 2001 Jan;296(1):181-7.
- 125. IUBMB Life. 2008 Jun;60(6):355-61.
- 126. J Rheumatol. 2008 Mar;35(3):407-13.
- 127. Am J Cardiol. 2001 Nov 15;88(10):1139-42.
- 128. Scand J Rheumatol. 1992;21(4):178-85.
- 129. J Nutr Sci Vitaminol (Tokyo). 1995 Apr;41(2):217-25.
- 130. Prostaglandins Leukot Essent Fatty Acids. 1998 Mar;58(3):185-91.
- 131. Clin Dev Immunol. 2004 Mar;11(1):13-21.
- 132. Int Immunopharmacol. 2001 Nov;1(12):2197-9.
- 133. Crit Care Med. 2004 Oct;32(10):2097-103.
- 134. Biochem Pharmacol. 2000 Feb 15;59(4):357-67.

- 135. Mediators Inflamm. 2006;5:30490.
- 136. Arch Pharm Res. 2002 Oct;25(5):561-71.
- 137. J Cell Biochem. 2004 Feb 1;91(2):232-42.
- 138. Am J Clin Nutr. 2004 Sep;80(3):649-55.
- 139. J Pharmacol Sci. 2008 Jun;107(2):128-37.
- 140. J Clin Endocrinol Metab. 2003 Oct;88(10):4623-32.
- 141. Arthritis Res. 1999;1:63-70.
- 142. QJM. 2002;95:787-96.
- 143. J Coll Physicians Surg Pak. 2004 Nov;14(11):673-6.
- 144. N Engl J Med. 2000 May 11;342(19):1392-8.
- 145. Int J Clin Pharmacol Ther Toxicol. 1990 Apr;28(4):153-7.
- 146. Atherosclerosis. 1982 Oct;45(1):1-10.
- 147. J Nutr. 2004 May;134(5):1181-5.
- 148. Mol Nutr Food Res. 2005 Jun;49(6):594-600.
- 149. Life Extension. 2008 Apr;14(3):37-43.
- 150. Proc Natl Acad Sci USA. 2002 Nov 26;99(24):15596-601.
- 151. J Endocrinol Invest. 2007 Jun;30(6):451-8.
- 152. Clin Endocrinol (Oxf). 2007 Mar;66(3):394-8.
- 153. Endocrinol Metab Clin North Am. 2007 Jun;36(2):365-77.
- 154. Arthritis Rheum. 2002 Nov;46(11):2924-7.
- 155. J Rheumatol. 1998 Feb;25(2):285-9.
- 156. World J Urol. 2003 Nov;21(5):346-55.
- 157. Compend Contin Educ Dent. 2004; Sep; 25(9):681-2.
- 158. J Clin Periodontol. 2008 Apr;35(4):277-90.
- 159. Arch Intern Med. 2008 Jun 9;168(11):1174-80.
- 160. Arch Intern Med. 2008 Jun 23;168(12):1340-9.
- 161. Am J Clin Nutr. 1999 May;69(5):842-56.
- 162. Curr Osteoporos Rep. 2006 Sep;4(3):96-102.
- 163. http://healthnews.uc.edu/news/?/757/.

- 164. World J Gastroenterol. 2005 Nov 14;11(42):6722-4.
- 165. Pharmazie. 2005 Oct;60(10):765-71.
- 166. Thromb Haemost. 2004 Feb;91(2):373-80.
- 167. J Thromb Haemost. 2004 Dec;2(12):2118-32.
- 168. Thromb Haemost. 1998 Jun;79(6):1116-8.
- 169. Thromb Res. 2004;113(3-4):205-9.
- 170. Am J Health Syst Pharm. 2005 Aug 1;62(15):1574-81.
- 171. Atherosclerosis. 2008 Jul 19.
- 172. Blood. 2007 Apr 1;109(7):2823-31.
- 173. J Vasc Res. 2008;45(5):427-36.
- 174. J Nutr. 2004 Nov;134(11):3100-5.
- 175. J Bone Miner Metab. 2000 18(4):216-22.
- 176. J Thromb Haemost. 2007 Dec;5(12):2503-11.
- 177. Arch Intern Med. 2006 Jun 26;166(12):1256-61.
- 178. Vitam Horm. 2008;78:393-416.
- 179. Thromb Haemost. 2004;92(5):1018-24.
- 180. Blood. 2007 Apr 15;109(8):3279-83.
- 181. Nutrition. 2001 Apr;17(4):315-21.
- 182. Int J Epidemiol. 2000 Oct;29(5):832-6.
- 183. Circulation. 1998 Mar 24;97(11):1029-36.
- 184. Am J Cardiol. 2008 Nov 17;102(10 Suppl):1K-34K.
- 185. Neurology. 2008 Sep 30;71(14):1057-64.
- 186. J Am Geriatr Soc. 2006 Mar;54(3):413-20.
- 187. Stroke. 2008 Dec;39(12):3145-51.
- 188. JAMA. 2007 Jul 18;298(3):309-16.
- 189. JAMA. 2008 Nov 12;300(18):2142-52.
- 190. JAMA. 2007 Jul 18;298(3):299-308.
- 191. Am J Cardiol. 2008 Oct 15;102(8):1040-5.
- 192. Exp Clin Endocrinol Diabetes. 2005 Feb;113(2):80-4.

- 193. Br J Clin Pharmacol. 2008 Sep 19.
- 194. J Agric Food Chem. 2005 Apr 6;53(7):2446-50.
- 195. Nutrition. 2005 Jul-Aug;21(7-8):848-54.
- 196. J Am Diet Assoc. 2005 Jan;105(1):65-71.
- 197. Altern Med Rev. 2004 Mar;9(1):63-9.
- 198. www.americanheart.org/presenter.jhtml?identifier=4632.
- 199. Am J Clin Nutr. 2000 Aug;72(2):389-94.
- 200. Am J Cardiol. 2000 Nov 1;86(9):943-9.
- 201. Expert Opin Pharmacother. 2008 May;9(7):1237-48.
- 202. Curr Cardiol Rep. 2003 Nov;5(6):470-6.
- 203. Br J Nutr. 2005 Apr;93(4):543-7.
- 204. Atherosclerosis. 2006 Apr;185(2):313-9.
- 205. J Nutr. 2002 Jul;132(7):1879-85.
- 206. J Nutr. 2005 Jun;135(6):1339-42.
- 207. J Am Coll Cardiol. 2005 Jul 5;46(1):120-4.
- 208. Am J Cardiol. 2007 Jan 15;99(2):154-8.
- 209. J Nutr Sci Vitaminol (Tokyo). 2003 Aug;49(4):270-6.
- 210. Lipids. 1998 Jun;33(6):567-72.
- 211. Biosci Biotechnol Biochem. 1995 Dec;59(12):2198-202.
- 212. Eur J Clin Nutr. 1993 Sep;47(Suppl 1):S85-90.
- 213. Neurology. 2007 Feb 20;68(8):563-8.
- 214. J Clin Endocrinol Metab. 2006 Nov;91(11):4433-7.
- 215. Neuro Endocrinol Lett. 2007 Apr;28(2):182-6.
- 216. Aging Male. 2004 Sep;7(3):197-204.
- 217. J Am Coll Cardiol. 2007 Sep 11;50(11):1070-6.
- 218. Biochem Biophys Res Commun. 2002 Sep 6;296(5):1051-7.
- 219. Handb Exp Pharmacol. 2005;170:537-61.
- 220. J Intern Med. 2008 Sep;264(3):245-53.
- 221. Menopause. 2006 Jul;13(4):643-50.

- 222. Eur J Cancer Prev. 2002 Aug;11(Suppl 2):S48-57.
- 223. Pharmacol Res. 2007 Aug;56(2):140-7.
- 224. J Steroid Biochem Mol Biol. 1993 Sep;46(3):381-8.
- 225. J Nutr. 1996 Apr;126(4):842-8.
- 226. Int J Obes. 1991 Nov;15(11):791-5.
- 227. Int J Impot Res. 2007 Sep;19(5):448-57.
- 228. Med Hypotheses. 1999 Jan;52(1):49-51.
- 229. Diabetes Care. 2007 Feb;30(2):318-24.
- 230. J Natl Cancer Inst. 2009 Jan 7;101(1):48-60.
- 231. N Engl J Med. 1998 Jul 23;339(4):229-34.
- 232. JAMA. 2002 Dec 4;288(21):2709-16.
- 233. Exp Clin Endocrinol Diabetes. 2005 Feb;113(2):80-4.
- 234. N Engl J Med. 1996 Jan 25;334(4):269-70.
- 235. Eur J Clin Invest. 1998 Jun;28(6):441-6.
- 236. J Androl. 2009 Jan-Feb;30(1):23-32.
- 237. Gerontology. 2008;54(3):153-6.
- 238. Circ Res. 2000 Nov 10;87(10):840-4.
- 239. Arch Mal Coeur Vaiss. 2006 Oct;99(10):915-21.
- 240. Trends Neurosci. 2004 May;27(5):283-9.
- 241. Nitric Oxide. 2006 Nov;15(3):259-63.
- 242. Nitric Oxide. 2006 Sep;15(2):93-102.
- 243. Proc Natl Acad Sci USA. 2005 Mar 29;102(13):4896-901.
- 244. J Agric Food Chem. 2006 Mar 8;54(5):1928-35.
- 245. Drugs Exp Clin Res. 2002;28(2-3):49-62.
- 246. J Nutr. 2001 Aug;131(8):2082-9.
- 247. Br J Pharmacol. 2005 Jul;145(6):767-74.
- 248. J Nutr Biochem. 2005 Sep;16(9):570-6.
- 249. JAMA. 2003 Aug 27;290(8):1030-1.
- 250. Eur Ann Allergy Clin Immunol. 2007 Feb;39(2):45-50.

- 251. Curr Med Chem. 2008;15(18):1840-50.
- 252. Arch Biochem Biophys. 2008 Aug 15;476(2):102-6.
- 253. www.circ.ahajournals.org/cgi/reprint/CIRCULATIONAHA.108.191261.
- 254. Semin Thromb Hemost. 2002;28(Suppl 2):3-13.
- 255. Zhonghua Yi Xue Za Zhi. 2006 Mar 14;86(10):678-80.
- 256. Am Heart J. 2005 Apr;149(4):606-12.
- 257. N Engl J Med. 2000 Oct 19;343(16):1139-47.
- 258. N Engl J Med. 2000 Oct 19;343(16):1179-82.
- 259. Arterioscler Thromb Vasc Biol. 2004 Sep;24(9):1734-40.
- 260. Circulation. 2003 Jul 15;108(2):155-60.
- 261. Am J Clin Nutr. 1996 Jan;63(1):116-22.
- 262. Am J Clin Nutr. 2006 Mar;83(3):567-74; quiz 726-7.
- 263. Nutrition. 2003 Mar;19(3):261-4.
- 264. Free Radic Res. 2006 Jan;40(1):85-94.
- 265. Drugs Exp Clin Res. 1978;4:49-53
- 266. Med Hypotheses. 1980;6(11):1123-33.
- 267. Clin Sci (Lond). 1994 Jan;86(1):43-8.
- 268. South Med J. 2008 Sep;101(9):918-24.
- 269. J Manag Care Pharm. 2007 Jun;13(5 Suppl):S3-5.
- 270. Am Heart J. 2006 Nov;152(5):867-75.
- 271. Hypertension. 2006 Feb;47(2):296-308.
- 272. JAMA. 2003 May 21;289(19):2560-72.
- 273. www.merck.com/product/usa/pi_circulars/c/cozaar/cozaar_pi.pdf.
- 274. www.benicar.com/pdf/prescribing_information.pdf.
- 275. Comp Biochem Physiol C. 1990;96(2):367-71.
- 276. Am J Hypertens. 2004 Nov;17(11 Pt 1):1056-8.
- 277. J Jpn Soc Nutr Food Sci. 1992;45:513-7.
- 278. Atherosclerosis. 2001 Sep;158(1):195-8.
- 279. Circulation. 1989;80(5):1320-7.

- 280. Eur J Public Health. 2004 Sept;14(3):235-9.
- 281. Epidemiology. 1992;3:194-202.
- 282. Lancet. 1999;354(9195):355-64.
- 283. Circulation. 1998;97:2222-9.
- 284. J Nutr. 2005 Nov;135(11):2739S-48S.
- 285. J Steroid Biochem Mol Biol. 2005 Jun;96(1):59-66.
- 286. N Engl J Med. 1989 Apr 20;320(16):1037-43.
- 287. Clin Exp Pharmacol Physiol. 1991 May;18(5):265-8.
- 288. Circulation. 1993 Aug;88(2):523-33.
- 289. Am J Clin Nutr. 1999 Nov;70(5):817-25.
- 290. Mol Aspects Med. 1994;15(Suppl):S265-72.
- 291. J Hum Hypertens. 1999 Mar;13(3):203-8.
- 292. Mol Aspects Med. 1994;15(Suppl):S257-63.
- 293. FASEB. 2006;20:A305.
- 294. Clin Sci (Lond). 2004 Nov;107(5):513-7.
- 295. Ann Pharmacother. 2008 Dec;42(12):1766-71.
- 296. Am J Clin Nutr. 1997;65(Suppl):712S-716S.
- 297. http://dashdiet.org/.
- 298. N Engl J Med. 2001 Jan 4;344(1):3-10.
- 299. Arch Fam Med. 1999 May-Jun;8(3):228-36.
- 300. J Cardiovasc Pharmacol. 2001 Oct;38(Suppl 1):S69-74.
- 301. Ann Intern Med. 2006 Apr 4;144(7):485-95.
- 302. Autoimmun Rev. 2008 Jul;7(7):558-66.
- 303. J Am Coll Cardiol. 1999 Oct;34(4):1208-15.
- 304. J Nutr. 2001 Feb;131(2):366S-8S.
- 305. Life Sci. 2000;66(2):161-71.
- 306. Nutrition. 2008 Oct;24(10):1030-8.
- 307. Antioxid Redox Signal. 2000;2(3):491-506.
- 308. Proc Natl Acad Sci USA. 1991 Mar 1;88(5):1646-50.

309. J Nutr. 2005b May;135(5):969-72.

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