

LE Magazine October 2006

On The COVER

When Homocysteine Levels Won't Come Down

By William Faloon



Twenty-five years ago, the Life Extension Foundation warned its members about the dangers of elevated homocysteine. Since then, excess homocysteine has been correlated with common disorders that include Alzheimer's disease,¹⁻⁸ osteoporosis,^{9,10} heart disease,¹¹⁻¹⁸ stroke,^{3,19,20} depression,²¹⁻²³ and cognitive impairment.²⁴⁻³⁸

A simple blood test can measure one's homocysteine level. If homocysteine blood levels exceed 7-8 $\mu\text{mol/L}$,³⁹ increasing one's intake of folic acid,⁴⁰⁻⁴⁹ vitamin B12,^{50,51} vitamin B6,^{41-44,49} and/or TMG (trimethylglycine)⁵²⁻⁵⁵ usually reduces homocysteine to safe ranges.

Over the past six months, we have received calls from some of our medical advisors and members who report incidences of stubbornly high homocysteine levels, despite aggressive use of homocysteine-lowering nutrients.

While investigating what could be done for these people, I had my own blood tested and was shocked to find my homocysteine had skyrocketed to 15.6 $\mu\text{mol/L}$, a level that puts me at higher risk for a host of age-related diseases. Serendipitously, I was interacting with our doctors to develop a protocol for members whose homocysteine remains persistently elevated even when high doses of nutrients like folic acid and B6 are ingested.

The encouraging news is that we have been able to identify reversible causes of excess homocysteine occurring in otherwise healthy individuals. Now that these mechanisms are better understood, most members should be able to keep their homocysteine levels in optimal ranges.

KIDNEY FUNCTION, CARDIOVASCULAR RISK, AND HOMOCYSTEINE LEVELS

It has long been known that those with severe kidney disease have startlingly high homocysteine levels and very high rates of cardiovascular disease. A number of published papers have discussed how excess accumulation of homocysteine in the blood of dialysis patients is one reason for the epidemic of cardiovascular mortality observed in these individuals.⁵⁶⁻⁷⁰ In fact, the risk of cardiovascular disease in chronic kidney disease is up to 30 times that of the general population!⁷¹

Recently, scientists have begun to publish papers describing cases of excess homocysteine in people with even mild kidney impairment.⁷²⁻⁷⁸ What most doctors don't know is that the kidneys facilitate the removal of homocysteine from the blood.^{79,80} The kidneys are also involved in enzymatic reactions that transform homocysteine into safer substances in the body.⁸¹ Any impairment in kidney function can result in excess homocysteine accumulation, even when one takes large quantities of classic homocysteine-lowering supplements.

As soon as I saw my homocysteine reading of 15.6 despite my very aggressive homocysteine-lowering strategy (with high-dose B vitamins), I knew I had a kidney problem. At first, even nephrologists (kidney specialists) did not think there was anything wrong with my kidneys. I had to inform these doctors of published scientific studies showing that if one takes high doses of homocysteine-lowering nutrients and homocysteine levels remain elevated, this indicates an underlying kidney problem.⁸²⁻⁸⁶

In those with kidney disease, homocysteine levels can remain at dangerously high levels despite supplementation with vitamins B6 and B12, folic acid, and TMG.^{85,87-91} Some people with end-stage kidney disease may not be able to reduce their homocysteine even with doses of folic acid as high as 60,000 mcg per day!⁹²

I DEMANDED MORE SOPHISTICATED KIDNEY FUNCTION TESTS

The most widely used screening tool for evaluating kidney function is the creatinine blood test. Most standard CBC/chemistry

blood profiles include the creatinine test to evaluate kidney function.

According to standard reference ranges, a creatinine blood level of up to 1.5 mg/dL is considered normal. My creatinine level was 1.3, which made my doctors initially question why I thought my kidneys were impaired. I had to remind them that I was taking massive doses of folic acid and vitamins B12 and B6. That meant my homocysteine reading should have been below 8 $\mu\text{mol/L}$, whereas in fact it was a startlingly high 15.6. The only reason my homocysteine could be this high, I argued, was a failure of my kidneys to remove and neutralize the excess homocysteine.

Fortunately, one of our scientific advisors enlightened me to a new blood test called Cystatin-C that provides a far more accurate measure of kidney function. Cystatin-C readings of up to 0.91 mg/L are considered normal. When I tested my own Cystatin-C level, it turned out to be 0.95 mg/L. I was thus able to document for my kidney specialist that I indeed had early-stage kidney impairment.

WHAT CAUSES SO MANY KIDNEYS TO FAIL

Most people over the age of 65 suffer from some degree of kidney dysfunction. Symptoms are usually not present, but blood tests show that a lot of otherwise healthy aging individuals have less-than-optimal kidney function. This fact is not widely recognized by mainstream medical doctors.

Kidney disorders are very common in diabetics.^{93,94} Those suffering from atherosclerosis,^{95,96} chronic inflammation,⁹⁷⁻¹⁰⁰ hypertension,¹⁰¹⁻¹⁰³ and certain other disorders also often display diminished kidney function.

In my case, I suffered from none of the underlying medical disorders known to cause kidney impairment. I was, however, taking relatively high doses of the anti-inflammatory drug ibuprofen for its cancer-preventive and sleep-inducing effects. Quite a bit of science supports the anti-cancer effects of drugs like ibuprofen.¹⁰⁴⁻¹⁰⁸ Regrettably, however, some people's kidneys cannot handle the side effects of ibuprofen, and I turned out to be one of them. The good news is that within two months of discontinuing the use of ibuprofen, my creatinine level dropped to 1.0 mg/dL (from 1.3) and my Cystatin-C declined to 0.75 mg/L (from 0.95). It appears that ibuprofen was the culprit, though the FDA does not mandate a kidney warning to be included on the label of these drugs. A quick search of the scientific literature, however, reveals potential risk to the kidneys with long-term ibuprofen use.¹⁰⁹⁻¹¹²



Based on our review of the published scientific literature, we are now advising members to pay very close attention to their blood indicators of kidney function. In my case, creatinine levels had risen from 0.8 mg/dL in January 2005 to 1.3 in November 2005—a clear indication that my kidneys were heading downhill. Keeping copies of previous blood tests and comparing the magnitude (or velocity) of change in certain biomarkers can help you identify newly emerging problems.

In addition to the standard blood markers of kidney function (creatinine, BUN, BUN/creatinine ratio), excessive homocysteine in someone taking homocysteine-lowering supplements is also an indication of potential kidney impairment.

Life Extension members already take supplements to protect their kidneys, such as coenzyme Q10,¹³⁶⁻¹³⁸ carnitine,¹³⁹⁻¹⁴³ taurine,¹⁴⁴⁻¹⁴⁷ curcumin,¹⁴⁸⁻¹⁵³ and others. We have published an extensive protocol on the prevention and treatment of kidney disease in our Disease Prevention and Treatment reference book.

HOW TO SUPPRESS STUBBORNLY HIGH HOMOCYSTEINE

The aging process often inhibits one's ability to maintain optimal homocysteine levels. For most people, however, the proper use of folic acid, vitamins B6 and B12, and/or TMG will bring homocysteine down to safe ranges.

Several years ago, I learned that I needed exceptionally high doses of homocysteine-lowering nutrients compared to most people. For instance, while 100 mg of vitamin B6 is all most people need, I required around 1000 mg/day of vitamin B6 to suppress my homocysteine adequately.



Based on what we now know, improving kidney function is another way to reduce homocysteine blood concentrations. In my case, as my blood indicators of kidney function improved (in response to halting the use of ibuprofen), my homocysteine levels steadily declined. I was finally able to lower my homocysteine to the optimal range of below 7-8 $\mu\text{mol/L}$ by taking additional TMG and a new prescription drug that I will describe next.

It is important to remember that I have a genetic predisposition to high homocysteine and have historically had to take large amounts of B vitamins to keep my homocysteine level around 8. Most members respond to homocysteine-lowering supplements much better than I do.

Fortunately, there is a form of folic acid for people like me whose bodies do not properly break down homocysteine. I am going to tell you all kinds of positive data about this form of folic acid, but the best news is that most of you do not even need it.

Ibuprofen and Cancer Prevention

Studies show that people who regularly use pain relievers like ibuprofen have sharply reduced risks of esophageal,^{113,114} brain,¹¹⁵ colon,^{114,117} prostate,¹¹⁴ and other cancers.^{114,117} Ibuprofen's mechanism of action is thought to be its inhibiting effects on the cyclooxygenase-2 (COX-2) enzyme. Cancer cells use COX-2 as biological fuel to propagate, and studies find that suppressing COX-2 may indeed reduce cancer risk.¹¹⁸ Fortunately, safe nutrients like curcumin also suppress COX-2, but do not inflict damage to the liver or kidneys.

Regular users of drugs like ibuprofen have reduced risks of Alzheimer's disease.¹¹⁹⁻¹²⁴ Fortunately, nutrients such as gamma tocopherol,¹²⁵⁻¹²⁷ curcumin,¹²⁸⁻¹³⁰ fish oil,¹³⁰⁻¹³² and resveratrol¹³³⁻¹³⁵ may also protect against Alzheimer's without inducing the toxic side effects associated with ibuprofen.

When Homocysteine Levels Won't Come Down

By William Faloon

A DIFFERENT KIND OF FOLIC ACID

When you consume folic acid, it goes through several metabolic steps before being converted to Metafolin®, which is the active form of folate in the body that actually reduces homocysteine. Some people fail to convert folic acid to L-methylfolate, which results in them accumulating higher-than-desired levels of homocysteine.

A patented form of folic acid called Metafolin® provides enormous benefits for those who do not naturally produce enough L-methylfolate. L-methylfolate is available both as a dietary supplement and as a prescription drug called Cerefolin®. The manufacturer of Cerefolin® claims that L-methylfolate reduces homocysteine almost three times more than folic acid.¹⁵⁴

Because Cerefolin® is a prescription drug, it is very expensive. The manufacturer's claims, however, appear to be somewhat embellished. The study cited by the manufacturer (showing almost three times greater homocysteine reduction) compared one-time dosing of 5200 mcg of L-methylfolate to 5000 mcg of regular folic acid. Since Cerefolin® is absorbed much quicker than folic acid, it would be expected that one-time dosing of Cerefolin® would produce faster results.

What the manufacturer fails to mention is that dietary supplement users seeking to lower homocysteine usually take vitamin B12, vitamin B6, and sometimes TMG with their folic acid. If a group of dietary supplement users were compared to a group that took only L-methylfolate, there might be not be a significant average difference in homocysteine levels over the long term.

The key factor here is individual need. For people who are unable to efficiently convert folic acid to L-methylfolate in their bodies, the more expensive L-methylfolate product will benefit them tremendously. Most people, however, can achieve desired homocysteine reduction merely by taking enough conventional homocysteine-lowering supplements.

All of this points to the critical importance of having your blood tested to assess your homocysteine level. If you are taking high doses of homocysteine-lowering nutrients and your homocysteine level remains persistently high, then you should first make sure that you do not suffer from kidney impairment. Whether or not you suffer from kidney impairment, if your homocysteine remains persistently high, consider taking 800-5600 mcg of L-methylfolate two times a day to achieve at least some improvement.

WHERE TO OBTAIN L-METHYLFOLATE

The drug company Merck holds the patent on L-methylfolate and has set up a number of barriers that prevent it from being more widely available as a dietary supplement. Fortunately, a few supplement companies (such as Source Naturals) were able to overcome these hurdles and make L-methylfolate available without a prescription.

Remember, this form of folic acid is not required if the supplements you take are keeping your homocysteine below 7-8 µmol/L of blood. For those who take proper doses of folic acid, B12, B6, and TMG, but still suffer higher-than-optimal homocysteine, L-methylfolate may be the solution.

Some people need only 800 mcg twice a day of L-methylfolate to optimize homocysteine. Others will need much higher potencies of L-methylfolate and may want to consider asking their doctor to prescribe Cerefolin® at a dose of one to two tablets daily. Each tablet of Cerefolin® provides:

- L-methylfolate 5635 mcg
- Vitamin B12 1000 mcg
- Vitamin B6 50 mg
- Vitamin B2 5 mg

Cerefolin® can be obtained in pharmacies and some insurance companies may cover it. The downside is that you have to get your doctor to prescribe it.

The Life Extension Buyers club offers Source Naturals' L-methylfolate supplement to members at a discount off the retail price. The trade name of this supplement is Metafolin® and it comes in bottles containing 120 800-mcg tablets. The retail price is \$17.98 per bottle, but members of the Life Extension Foundation can obtain it for only \$12.50. Please remember that L-methylfolate is for those who are unable to lower their homocysteine with lower-cost conventional supplements. Most people do not need it.

Nutrients That Keep Homocysteine Levels Low

Most members are already supplementing with nutrients that adequately suppress homocysteine levels. The minimum doses we recommend to control homocysteine are:

- Folic acid — 800 mcg
- Vitamin B12 — 300 mcg
- Vitamin B6 — 100 mg
- TMG (trimethylglycine) — 500 mg

Those with a homocysteine level over 7-8 $\mu\text{mol/L}$ of blood should consider daily supplementation with:

- Folic acid — 1600-3200 mcg
- Vitamin B12 — 1000-2000 mcg
- Vitamin B6 — 250-1000 mg
- TMG — 4000-8000 mg

(Watch out for symptoms of peripheral neuropathy when B6 daily doses exceed 200 mg for an extended period. This is a rare occurrence, but it has been reported in mainstream medical journals.)

If homocysteine levels remain persistently elevated despite high-dose supplementation with these nutrients, carefully monitor kidney function and take 1600-11,000 mcg a day of L-methylfolate.

BLOOD TESTING PROBABLY SAVED MY LIFE

Had I not had regular blood tests performed, I would have assumed that the nutrients I took every day were adequately suppressing my homocysteine levels. I was fortunate to learn a long time ago that I needed a lot of vitamin B6 to reduce my homocysteine to safe ranges.

The blood tests I took in November 2005 alerted me to an underlying kidney disorder that I was able to reverse simply by discontinuing a drug (ibuprofen). Many other drugs can adversely affect the liver, kidneys, and bone marrow. A CBC/chemistry blood test reveals drug-induced pathologies before they cause irreversible damage. If I had not taken this blood test, I may have continued taking ibuprofen for its sleep-inducing and cancer-preventive effects. Since early-stage renal failure does not usually present symptoms, I could have suffered irreversible kidney damage, along with the life-threatening complications—such as sharply increased risk for heart attack and stroke—caused by that kidney disease.

Kidney disease is a leading cause of death in the United States, yet most cases of renal dysfunction are preventable if annual blood tests are taken to rule out factors such as diabetes, drug-induced toxicities, early-stage atherosclerosis, and chronic inflammation.

Recommended Blood Tests for Men and Women

MALE PANEL

- CBC/Chemistry
- Total Testosterone
- DHEA
- Free Testosterone
- PSA (prostate-specific antigen)
- Estradiol
- Homocysteine
- C-Reactive Protein

FEMALE PANEL

- CBC/Chemistry
- Total Testosterone
- DHEA
- Free Testosterone
- Estradiol (an estrogen)
- Progesterone
- Homocysteine
- C-Reactive Protein

To order these blood tests for yourself, call **1-800-208-3444** (24 hours a day). The member price for the Male or Female Panel is \$299.

By making this one phone call, you will be sent a requisition form and list of blood drawing stations in your area. Most of the time, no appointment is necessary. This means that you can pick a time convenient to you to have your blood drawn.

The test results are usually mailed to you in 7-10 days. If you have any questions, Life Extension's health advisors are available by calling **1-800-226-2370**.

DISCOUNT BLOOD TESTING AVAILABLE TO FOUNDATION MEMBERS

Since the early 1980s, Life Extension has advised its members to have annual blood tests to identify disease risk factors that can be reversed before serious illness develops.

Some members are able to obtain blood tests from their doctors. A problem that I frequently encounter is that even when doctors order all the blood tests requested, the phlebotomist often fails to check off the appropriate codes on the laboratory requisition form or does not properly draw the blood. When the results come back incomplete, another blood draw becomes necessary, thus inconveniencing the patient.

Even today, many doctors still refuse to prescribe blood tests for important cardiovascular risk factors such as homocysteine and C-reactive protein. Life Extension resolved this problem 10 years ago by offering blood tests directly to its members.

Members can obtain blood tests for a fraction of the price charged by commercial laboratories. For example, the comprehensive Male or Female Panels cost around \$1,100 at a commercial laboratory, yet Foundation members can obtain these identical tests for only \$299.

Based on what I have discovered as a result of having my own blood tested regularly, I am convinced that I have corrected a number of genetic risk factors that would have predisposed me to a premature death. Whether using your own doctor, a commercial laboratory, or our blood-testing service, I encourage every member to have his or her blood tested at least once a year.

For longer life,



William Faloon

References

1. Religa D, Styczynska M, Peplonska B, et al. Homocysteine, apolipoprotein E and methylenetetrahydrofolate reductase in Alzheimer's disease and mild cognitive impairment. *Dement Geriatr Cogn Disord*. 2003;16(2):64-70.
2. Selley ML. Increased concentrations of homocysteine and asymmetric dimethylarginine and decreased concentrations of nitric oxide in the plasma of patients with Alzheimer's disease. *Neurobiol Aging*. 2003 Nov;24(7):903-7.
3. McIlroy SP, Dynan KB, Lawson JT, Patterson CC, Passmore AP. Moderately elevated plasma homocysteine, methylenetetrahydrofolate reductase genotype, and risk for stroke, vascular dementia, and Alzheimer disease in Northern Ireland. *Stroke*. 2002 Oct;33(10):2351-6.

4. Reutens S, Sachdev P. Homocysteine in neuropsychiatric disorders of the elderly. *Int J Geriatr Psychiatry*. 2002 Sep;17(9):859-64.
5. Joosten E. Homocysteine, vascular dementia and Alzheimer's disease. *Clin Chem Lab Med*. 2001 Aug;39(8):717-20.
6. Miller JW. Homocysteine, Alzheimer's disease, and cognitive function. *Nutrition*. 2000 Jul;16(7-8):675-7.
7. McCaddon A, Davies G, Hudson P, Tandy S, Cattell H. Total serum homocysteine in senile dementia of Alzheimer type. *Int J Geriatr Psychiatry*. 1998 Apr;13(4):235-9.
8. Gottfries CG, Lehmann W, Regland B. Early diagnosis of cognitive impairment in the elderly with the focus on Alzheimer's disease. *J Neural Transm*. 1998;105(8-9):773-86.
9. van Meurs JB, Dhonukshe-Rutten RA, Pluijm SM, et al. Homocysteine levels and the risk of osteoporotic fracture. *N Engl J Med*. 2004 May 13;350(20):2033-41.
10. McLean RR, Jacques PF, Selhub J, et al. Homocysteine as a predictive factor for hip fracture in older persons. *N Engl J Med*. 2004 May 13;350(20):2042-9.
11. Kazemi MB, Eshraghian K, Omrani GR, Lankarani KB, Hosseini E. Homocysteine level and coronary artery disease. *Angiology*. 2006 Jan;57(1):9-14.
12. Adachi H, Hirai Y, Fujiura Y, et al. Plasma homocysteine levels and atherosclerosis in Japan: epidemiological study by use of carotid ultrasonography. *Stroke*. 2002 Sep;33(9):2177-81.
13. Auer J, Berent R, Weber T, Lassnig E, Eber B. Homocysteine and cardiovascular risk. *Wien Med Wochenschr*. 2001;151(1-2):25-8.
14. Beaudoux JL, Jacob N, Giral P, Foglietti MJ, Bruckert E. New non-lipidic biological markers of atherosclerosis. *Ann Med Interne (Paris)*. 2001 Apr;152(3):169-79.
15. Aronow WS. Association between plasma homocysteine and vascular atherosclerotic disease in older persons. *Prev Cardiol*. 2000;3(2):89-91.
16. Dzielinska Z, Kadziela J, Sitkiewicz D, et al. Elevated levels of homocysteine in plasma as a risk factor for coronary artery disease. *Pol Arch Med Wewn*. 2000 Jul;104(1):345-53.
17. Bomalaski PS. Homocysteine: a risk factor of atherosclerosis. *Nurse Pract*. 2000 Apr;25(4):129-31.
18. Stampfer MJ, Malinow MR, Willett WC, et al. A prospective study of plasma homocyst(e)ine and risk of myocardial infarction in US physicians. *JAMA*. 1992 Aug 19;268(7):877-81.
19. Sachdev PS, Valenzuela MJ, Brodaty H, et al. Homocysteine as a risk factor for cognitive impairment in stroke patients. *Dement Geriatr Cogn Disord*. 2003;15(3):155-62.
20. bdel-Raheem MM, Hebert B, Potti A, Koka VK, Danielson BD. Hyperhomocysteinemia and the risk of thromboembolic phenomenon in patients with chronic renal failure. *Thromb Res*. 2002 Feb 15;105(4):299-302.
21. Bjelland I, Tell GS, Vollset SE, Refsum H, Ueland PM. Folate, vitamin B12, homocysteine, and the MTHFR 677C->T polymorphism in anxiety and depression: the Hordaland Homocysteine Study. *Arch Gen Psychiatry*. 2003 Jun;60(6):618-26.
22. Naismith S, Hickie I, Ward PB, et al. Caudate nucleus volumes and genetic determinants of homocysteine metabolism in the prediction of psychomotor speed in older persons with depression. *Am J Psychiatry*. 2002 Dec;159(12):2096-8.
23. Kuo HK, Sorond FA, Chen JH, Hashmi A, Milberg WP, Lipsitz LA. The role of homocysteine in multisystem age-related problems: a systematic review. *J Gerontol A Biol Sci Med Sci*. 2005 Sep;60(9):1190-201.
24. Nurk E, Refsum H, Tell GS, et al. Plasma total homocysteine and memory in the elderly: the Hordaland Homocysteine Study. *Ann Neurol*. 2005 Dec;58(6):847-57.

25. Teunissen CE, Blom AH, Van Boxtel MP, et al. Homocysteine: a marker for cognitive performance? A longitudinal follow-up study. *J Nutr Health Aging*. 2003;7(3):153-9.
26. Miller JW, Green R, Ramos MI, et al. Homocysteine and cognitive function in the Sacramento Area Latino Study on Aging. *Am J Clin Nutr*. 2003 Sep;78(3):441-7.
27. Ravaglia G, Forti P, Maioli F, et al. Homocysteine and cognitive function in healthy elderly community dwellers in Italy. *Am J Clin Nutr*. 2003 Mar;77(3):668-73.
28. Stewart R, Asonganyi B, Sherwood R. Plasma homocysteine and cognitive impairment in an older British African-Caribbean population. *J Am Geriatr Soc*. 2002 Jul;50(7):1227-32.
29. Prins ND, Den HT, Hofman A, et al. Homocysteine and cognitive function in the elderly: the Rotterdam Scan Study. *Neurology*. 2002 Nov 12;59(9):1375-80.
30. Budge MM, de JC, Hogervorst E, Smith AD. Total plasma homocysteine, age, systolic blood pressure, and cognitive performance in older people. *J Am Geriatr Soc*. 2002 Dec;50(12):2014-8.
31. Duthie SJ, Whalley LJ, Collins AR, et al. Homocysteine, B vitamin status, and cognitive function in the elderly. *Am J Clin Nutr*. 2002 May;75(5):908-13.
32. McCaddon A, Hudson P, Davies G, et al. Homocysteine and cognitive decline in healthy elderly. *Dement Geriatr Cogn Disord*. 2001 Sep;12(5):309-13.
33. Ventura P, Panini R, Verlato C, Scarpetta G, Salvioli G. Hyperhomocysteinemia and related factors in 600 hospitalized elderly subjects. *Metabolism*. 2001 Dec;50(12):1466-71.
34. Budge M, Johnston C, Hogervorst E, et al. Plasma total homocysteine and cognitive performance in a volunteer elderly population. *Ann NY Acad Sci*. 2000 Apr;903:407-10.
35. Kalmijn S, Launer LJ, Lindemans J, et al. Total homocysteine and cognitive decline in a community-based sample of elderly subjects: the Rotterdam Study. *Am J Epidemiol*. 1999 Aug 1;150(3):283-9.
36. Lehmann M, Gottfries CG, Regland B. Identification of cognitive impairment in the elderly: homocysteine is an early marker. *Dement Geriatr Cogn Disord*. 1999 Jan;10(1):12-20.
37. Smith AD. Homocysteine, B vitamins, and cognitive deficit in the elderly. *Am J Clin Nutr*. 2002 May;75(5):785-6.
38. Selhub J, Bagley LC, Miller J, Rosenberg IH. B vitamins, homocysteine, and neurocognitive function in the elderly. *Am J Clin Nutr*. 2000 Feb;71(2):614S-20S.
39. Robinson K, Mayer EL, Miller DP, et al. Hyperhomocysteinemia and low pyridoxal phosphate. Common and independent reversible risk factors for coronary artery disease. *Circulation*. 1995 Nov 15;92(10):2825-30.
40. Aisen PS, Egelko S, Andrews H, et al. A pilot study of vitamins to lower plasma homocysteine levels in Alzheimer disease. *Am J Geriatr Psychiatry*. 2003 Mar;11(2):246-9.
41. Bostom AG, Jacques PF, Liaugaudas G, et al. Total homocysteine lowering treatment among coronary artery disease patients in the era of folic acid-fortified cereal grain flour. *Arterioscler Thromb Vasc Biol*. 2002 Mar 1;22(3):488-91.
42. Lehmann M, Regland B, Blennow K, Gottfries CG. Vitamin B12-B6-folate treatment improves blood-brain barrier function in patients with hyperhomocysteinemia and mild cognitive impairment. *Dement Geriatr Cogn Disord*. 2003;16(3):145-50.
43. Schnyder G, Roffi M, Pin R, et al. Decreased rate of coronary restenosis after lowering of plasma homocysteine levels. *N Engl J Med*. 2001 Nov 29;345(22):1593-600.
44. Aleman G, Tovar AR, Torres N. Homocysteine metabolism and risk of cardiovascular diseases: importance of the nutritional status on folic acid, vitamins B6 and B12. *Rev Invest Clin*. 2001 Mar;53(2):141-51.
45. Nilsson K, Gustafson L, Hultberg B. Improvement of cognitive functions after cobalamin/folate supplementation in elderly

patients with dementia and elevated plasma homocysteine. *Int J Geriatr Psychiatry*. 2001 Jun;16(6):609-14.

46. Malinow MR, Duell PB, Hess DL, et al. Reduction of plasma homocyst(e)ine levels by breakfast cereal fortified with folic acid in patients with coronary heart disease. *N Engl J Med*. 1998 Apr 9;338(15):1009-15.

47. Tucker KL, Mahnken B, Wilson PW, Jacques P, Selhub J. Folic acid fortification of the food supply. Potential benefits and risks for the elderly population. *JAMA*. 1996 Dec 18;276(23):1879-85.

48. Verhoef P, Stampfer MJ, Buring JE, et al. Homocysteine metabolism and risk of myocardial infarction: relation with vitamins B6, B12, and folate. *Am J Epidemiol*. 1996 May 1;143(9):845-59.

49. Riggs KM, Spiro A, III, Tucker K, Rush D. Relations of vitamin B-12, vitamin B-6, folate, and homocysteine to cognitive performance in the Normative Aging Study. *Am J Clin Nutr*. 1996 Mar;63(3):306-14.

50. Hoffer LJ, Djahangirian O, Bourgouin PE, Eid J, Saboohi F. Comparative effects of hydroxocobalamin and cyanocobalamin on plasma homocysteine concentrations in end-stage renal disease. *Metabolism*. 2005 Oct;54(10):1362-7.

51. Elian KM, Hoffer LJ. Hydroxocobalamin reduces hyperhomocysteinemia in end-stage renal disease. *Metabolism*. 2002 Jul;51(7):881-6.

52. Available at: <http://www.lef.org/magazine/mag99/mar99-report2.html>. Accessed June 17, 2006.

53. Schwab U, Torronen A, Meririnne E, et al. Orally administered betaine has an acute and dose-dependent effect on serum betaine and plasma homocysteine concentrations in healthy humans. *J Nutr*. 2006 Jan;136(1):34-8.

54. Singh RH, Kruger WD, Wang L, Pasquali M, Elsas LJ. Cystathionine beta-synthase deficiency: effects of betaine supplementation after methionine restriction in B6-nonresponsive homocystinuria. *Genet Med*. 2004 Mar;6(2):90-5.

55. Schwab U, Torronen A, Toppinen L, et al. Betaine supplementation decreases plasma homocysteine concentrations but does not affect body weight, body composition, or resting energy expenditure in human subjects. *Am J Clin Nutr*. 2002 Nov;76(5):961-7.

56. Perna AF, Satta E, Acanfora F, et al. Increased plasma protein homocysteinylation in hemodialysis patients. *Kidney Int*. 2006 Mar;69(5):869-76.

57. Sjoberg B, Anderstam B, Suliman M, Alvestrand A. Plasma reduced homocysteine and other aminothiols concentrations in patients with CKD. *Am J Kidney Dis*. 2006 Jan;47(1):60-71.

58. Tsai JC, Kuo HT, Chiu YW, et al. Correlation of plasma homocysteine level with arterial stiffness and pulse pressure in hemodialysis patients. *Atherosclerosis*. 2005 Sep;182(1):121-7.

59. Preston E, Ellis MR, Kulinskaya E, Davies AH, Brown EA. Association between carotid artery intima-media thickness and cardiovascular risk factors in CKD. *Am J Kidney Dis*. 2005 Nov;46(5):856-62.

60. Foley RN, Wang C, Collins AJ. Cardiovascular risk factor profiles and kidney function stage in the US general population: the NHANES III study. *Mayo Clin Proc*. 2005 Oct;80(10):1270-7.

61. Siroka R, Trefil L, Rajdl D, et al. Asymmetric dimethylarginine, homocysteine and renal function—is there a relation? *Clin Chem Lab Med*. 2005;43(10):1147-50.

62. Maeda N, Sawayama Y, Tatsukawa M, et al. Carotid artery lesions and atherosclerotic risk factors in Japanese hemodialysis patients. *Atherosclerosis*. 2003 Jul;169(1):183-92.

63. Ohkuma T, Minagawa T, Takada N, et al. C-reactive protein, lipoprotein(a), homocysteine, and male sex contribute to carotid atherosclerosis in peritoneal dialysis patients. *Am J Kidney Dis*. 2003 Aug;42(2):355-61.

64. Mallamaci F, Zoccali C, Tripepi G, et al. Hyperhomocysteinemia predicts cardiovascular outcomes in hemodialysis patients. *Kidney Int*. 2002 Feb;61(2):609-14.

65. Kimura H and Yoshida H. Risk factors for atherosclerotic vascular disease in patients on maintenance hemodialysis--with

especial respect to reverse cholesterol transport system and hyperhomocysteinemia. *Rinsho Byori*. 2002 Aug;50(8):793-801.

66. Krasniak A, Drozd M, Chmiel G, et al. Evaluation of atherosclerosis progression in patients treated repeatedly with hemodialysis. *Przegl Lek*. 2002;59(8):606-10.

67. Lim PS, Hung WR, Wei YH. Polymorphism in methylenetetrahydrofolate reductase gene: its impact on plasma homocysteine levels and carotid atherosclerosis in ESRD patients receiving hemodialysis. *Nephron*. 2001 Mar;87(3):249-56.

68. Oishi K, Nagake Y, Yamasaki H, et al. The significance of serum homocysteine levels in diabetic patients on haemodialysis. *Nephrol Dial Transplant*. 2000 Jun;15(6):851-5.

69. Moustapha A, Naso A, Nahlawi M, et al. Prospective study of hyperhomocysteinemia as an adverse cardiovascular risk factor in end-stage renal disease. *Circulation*. 1998 Jan 20;97(2):138-41.

70. Bostom AG, Shemin D, Verhoef P, et al. Elevated fasting total plasma homocysteine levels and cardiovascular disease outcomes in maintenance dialysis patients. A prospective study. *Arterioscler Thromb Vasc Biol*. 1997 Nov;17(11):2554-8.

71. Parfrey PS, Foley RN. The clinical epidemiology of cardiac disease in chronic renal failure. *J Am Soc Nephrol*. 1999 Jul;10(7):1606-15.

72. Nanayakkara PW, Teerlink T, Stehouwer CD, et al. Plasma asymmetric dimethylarginine (ADMA) concentration is independently associated with carotid intima-media thickness and plasma soluble vascular cell adhesion molecule-1 (sVCAM-1) concentration in patients with mild-to-moderate renal failure. *Kidney Int*. 2005 Nov;68(5):2230-6.

73. Henry RM, Kostense PJ, Bos G, et al. Mild renal insufficiency is associated with increased cardiovascular mortality: The Hoorn Study. *Kidney Int*. 2002 Oct;62(4):1402-7.

74. Stam F, van Guldener C, Becker A, et al. Endothelial dysfunction contributes to renal function-associated cardiovascular mortality in a population with mild renal insufficiency: the Hoorn study. *J Am Soc Nephrol*. 2006 Feb;17(2):537-45.

75. McCullough PA, Soman SS, Shah SS, et al. Risks associated with renal dysfunction in patients in the coronary care unit. *J Am Coll Cardiol*. 2000 Sep;36(3):679-84.

76. Culeton BF, Larson MG, Wilson PW, et al. Cardiovascular disease and mortality in a community-based cohort with mild renal insufficiency. *Kidney Int*. 1999 Dec;56(6):2214-9.

77. Jungers P, Nguyen KT, Massy ZA, et al. Incidence of atherosclerotic arterial occlusive accidents in predialysis and dialysis patients: a multicentric study in the Ile de France district. *Nephrol Dial Transplant*. 1999 Apr;14(4):898-902.

78. McCullough PA, Wolyn R, Rocher LL, Levin RN, O'Neill WW. Acute renal failure after coronary intervention: incidence, risk factors, and relationship to mortality. *Am J Med*. 1997 Nov;103(5):368-75.

79. House JD, Brosnan ME, Brosnan JT. Renal uptake and excretion of homocysteine in rats with acute hyperhomocysteinemia. *Kidney Int*. 1998 Nov;54(5):1601-7.

80. House JD, Brosnan ME, Brosnan JT. Characterization of homocysteine metabolism in the rat kidney. *Biochem J*. 1997 Nov 15;328 (Pt 1):287-92.

81. Herrmann W, Obeid R. Hyperhomocysteinemia and response of methionine cycle intermediates to vitamin treatment in renal patients. *Clin Chem Lab Med*. 2005;43(10):1039-47.

82. Garibotto G, Sofia A, Valli A, et al. Causes of hyperhomocysteinemia in patients with chronic kidney diseases. *Semin Nephrol*. 2006 Jan;26(1):3-7.

83. Tunuguntla A, Yerra L. The renal patient with cardiovascular disease—no longer a simple plumbing problem. *Tenn Med*. 2005 Aug;98(8):395-6, 399.

84. Nerbass FB, Draibe SA, Feiten SF, et al. Homocysteine and its determinants in nondialyzed chronic kidney disease patients. *J Am Diet Assoc*. 2006 Feb;106(2):267-70.

85. Gonin JM, Nguyen H, Gonin R, et al. Controlled trials of very high dose folic acid, vitamins B12 and B6, intravenous folinic acid and serine for treatment of hyperhomocysteinemia in ESRD. *J Nephrol.* 2003 Jul;16(4):522-34.
86. Ghandour H, Bagley PJ, Shemin D, et al. Distribution of plasma folate forms in hemodialysis patients receiving high daily doses of L-folinic or folic acid. *Kidney Int.* 2002 Dec;62(6):2246-9.
87. Bostom AG, Culleton BF. Hyperhomocysteinemia in chronic renal disease. *J Am Soc Nephrol.* 1999 Apr;10(4):891-900.
88. Massy ZA. Potential strategies to normalize the levels of homocysteine in chronic renal failure patients. *Kidney Int Suppl.* 2003 May;(84):S134-6.
89. Vrentzos GE, Papadakis JA, Vardakis KE, et al. Intravenous administration of vitamin B12 in the treatment of hyperhomocysteinemia associated with end-stage renal disease. *J Nephrol.* 2003 Jul;16(4):535-9.
90. Righetti M, Ferrario GM, Milani S, et al. Effects of folic acid treatment on homocysteine levels and vascular disease in hemodialysis patients. *Med Sci Monit.* 2003 Apr;9(4):I19-24.
91. Polkinghorne KR, Zoungas S, Branley P, et al. Randomized, placebo-controlled trial of intramuscular vitamin B12 for the treatment of hyperhomocysteinemia in dialysis patients. *Intern Med J.* 2003 Nov;33(11):489-94.
92. Sunder-Plassmann G, Fodinger M, Buchmayer H, et al. Effect of high dose folic acid therapy on hyperhomocysteinemia in hemodialysis patients: results of the Vienna multicenter study. *J Am Soc Nephrol.* 2000 Jun;11(6):1106-16.
93. Available at: <http://www.duj.com/Kidneydisease.html>. Accessed June 17, 2006.
94. Barbosa J, Steffes MW, Sutherland DE, et al. Effect of glycemic control on early diabetic renal lesions. A 5-year randomized controlled clinical trial of insulin-dependent diabetic kidney transplant recipients. *JAMA.* 1994 Aug 24;272(8):600-6.
95. Sarnak MJ, Levey AS, Schoolwerth AC, et al. Kidney disease as a risk factor for development of cardiovascular disease: a statement from the American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. *Circulation.* 2003 Oct 28;108(17):2154-69.
96. Gale CR, Ashurst H, Phillips NJ, et al. Renal function, plasma homocysteine and carotid atherosclerosis in elderly people. *Atherosclerosis.* 2001 Jan;154(1):141-6.
97. Seliger SL. Inflammation and dyslipidemia in nephropathy: an epidemiologic perspective. *Kidney Int.* 2006 Jan;69(2):206-8.
98. az-Buxo JA, Woods HF. Protecting the endothelium: a new focus for management of chronic kidney disease. *Hemodial Int.* 2006 Jan;10(1):42-8.
99. Zhang R, Liao J, Morse S, Donelon S, Reisin E. Kidney disease and the metabolic syndrome. *Am J Med Sci.* 2005 Dec;330(6):319-25.
100. Fathi RB, Gurm HS, Chew DP, et al. The interaction of vascular inflammation and chronic kidney disease for the prediction of long-term death after percutaneous coronary intervention. *Am Heart J.* 2005 Dec;150(6):1190-7.
101. Chade AR, Brosh D, Higano ST, et al. Mild renal insufficiency is associated with reduced coronary flow in patients with non-obstructive coronary artery disease. *Kidney Int.* 2006 Jan;69(2):266-71.
102. Wenzel RR. Renal protection in hypertensive patients: selection of antihypertensive therapy. *Drugs.* 2005;65 Suppl 2:29-39.
103. Ibrahim MM. RAS inhibition in hypertension. *J Hum Hypertens.* 2006 Feb;20(2):101-8.
104. Harris RE, Chlebowski RT, Jackson RD, et al. Breast cancer and nonsteroidal anti-inflammatory drugs: prospective results from the Women's Health Initiative. *Cancer Res.* 2003 Sep 15;63(18):6096-101.
105. Jacobs EJ, Rodriguez C, Mondul AM, et al. A large cohort study of aspirin and other nonsteroidal anti-inflammatory drugs and prostate cancer incidence. *J Natl Cancer Inst.* 2005 Jul 6;97(13):975-80.
106. Thurnher D, Bakroeva M, Formanek M, Knerer B, Kornfehl J. Non-steroidal anti-inflammatory drugs inhibit telomerase

activity in head and neck squamous carcinoma cell lines. *Head Neck*. 2001 Dec;23(12):1049-55.

107. McMillan DC, Sattar N, Talwar D, O'Reilly DS, McArdle CS. Changes in micronutrient concentrations following anti-inflammatory treatment in patients with gastrointestinal cancer. *Nutrition*. 2000 Jun;16(6):425-8.
108. Alshafie GA, Harris RE, Robertson FM, et al. Comparative chemopreventive activity of ibuprofen and N-(4-hydroxyphenyl) retinamide against the development and growth of rat mammary adenocarcinomas. *Anticancer Res*. 1999 Jul;19(4B):3031-6.
109. Ulinski T, Bensman A. Renal complications of non-steroidal anti-inflammatories. *Arch Pediatr*. 2004 Jul;11(7):885-8.
110. Ulinski T, Guigonis V, Dunan O, Bensman A. Acute renal failure after treatment with non-steroidal anti-inflammatory drugs. *Eur J Pediatr*. 2004 Mar;163(3):148-50.
111. Perneger TV, Whelton PK, Klag MJ. Risk of kidney failure associated with the use of acetaminophen, aspirin, and nonsteroidal antiinflammatory drugs. *N Engl J Med*. 1994 Dec 22;331(25):1675-9.
112. Whelton A. Renal effects of over-the-counter analgesics. *J Clin Pharmacol*. 1995 May;35(5):454-63.
113. Vaughan TL, Dong LM, Blount PL, et al. Non-steroidal anti-inflammatory drugs and risk of neoplastic progression in Barrett's oesophagus: a prospective study. *Lancet Oncol*. 2005 Dec;6(12):945-52.
114. Harris RE, Beebe-Donk J, Doss H, Burr DD. Aspirin, ibuprofen, and other non-steroidal anti-inflammatory drugs in cancer prevention: a critical review of non-selective COX-2 blockade (review). *Oncol Rep*. 2005 Apr;13(4):559-83.
115. Sivak-Sears NR, Schwartzbaum JA, Miike R, Moghadassi M, Wrensch M. Case-control study of use of nonsteroidal antiinflammatory drugs and glioblastoma multiforme. *Am J Epidemiol*. 2004 Jun 15;159(12):1131-9.
116. Smith ML, Hawcroft G, Hull MA. The effect of non-steroidal anti-inflammatory drugs on human colorectal cancer cells: evidence of different mechanisms of action. *Eur J Cancer*. 2000 Mar;36(5):664-74.
117. Harris RE, Beebe-Donk J, Alshafie GA. Reduction in the risk of human breast cancer by selective cyclooxygenase-2 (COX-2) inhibitors. *BMC Cancer*. 2006;627.
118. Grau de Castro JJ. COX-2 inhibitors in cancer prevention. *Rev Clin Esp*. 2005 Sep;205(9):446-56.
119. Townsend KP, Pratico D. Novel therapeutic opportunities for Alzheimer's disease: focus on nonsteroidal anti-inflammatory drugs. *FASEB J*. 2005 Oct;19(12):1592-601.
120. Hirohata M, Ono K, Naiki H, Yamada M. Non-steroidal anti-inflammatory drugs have anti-amyloidogenic effects for Alzheimer's beta-amyloid fibrils in vitro. *Neuropharmacology*. 2005 Dec;49(7):1088-99.
121. Aizen E, Kagan G, Assy B, et al. Effect of non-steroidal anti-inflammatory drugs on natural killer cell activity in patients with dementia. *Isr Med Assoc J*. 2005 Feb;7(2):78-81.
122. Morihara T, Teter B, Yang F, et al. Ibuprofen suppresses interleukin-1beta induction of pro-amyloidogenic alpha1-antichymotrypsin to ameliorate beta-amyloid (Abeta) pathology in Alzheimer's models. *Neuropsychopharmacology*. 2005 Jun;30(6):1111-20.
123. Cole GM, Morihara T, Lim GP et al. NSAID and antioxidant prevention of Alzheimer's disease: lessons from in vitro and animal models. *Ann NY Acad Sci*. 2004 Dec;1035:68-84.
124. Dokmeci D. Ibuprofen and Alzheimer's disease. *Folia Med (Plovdiv)*. 2004;46(2):5-10.
125. Morris MC, Evans DA, Tangney CC, et al. Relation of the tocopherol forms to incident Alzheimer disease and to cognitive change. *Am J Clin Nutr*. 2005 Feb;81(2):508-14.
126. Frank B, Gupta S. A review of antioxidants and Alzheimer's disease. *Ann Clin Psychiatry*. 2005 Oct;17(4):269-86.
127. Williamson KS, Gabbita SP, Mou S, et al. The nitration product 5-nitro-gamma-tocopherol is increased in the Alzheimer brain. *Nitric Oxide*. 2002 Mar;6(2):221-7.

128. Kim H, Park BS, Lee KG, et al. Effects of naturally occurring compounds on fibril formation and oxidative stress of beta-amyloid. *J Agric Food Chem*. 2005 Nov 2;53(22):8537-41.
129. Lim GP, Chu T, Yang F, et al. The curry spice curcumin reduces oxidative damage and amyloid pathology in an Alzheimer transgenic mouse. *J Neurosci*. 2001 Nov 1;21(21):8370-7.
130. Cole GM, Lim GP, Yang F, et al. Prevention of Alzheimer's disease: Omega-3 fatty acid and phenolic anti-oxidant interventions. *Neurobiol Aging*. 2005 Dec;26 Suppl 1:133-6.
131. Bourre JM. Roles of unsaturated fatty acids (especially omega-3 fatty acids) in the brain at various ages and during ageing. *J Nutr Health Aging*. 2004;8(3):163-74.
132. Morris MC, Evans DA, Bienias JL, et al. Consumption of fish and n-3 fatty acids and risk of incident Alzheimer disease. *Arch Neurol*. 2003 Jul;60(7):940-6.
133. Marambaud P, Zhao H, Davies P. Resveratrol promotes clearance of Alzheimer's disease amyloid-beta peptides. *J Biol Chem*. 2005 Nov 11;280(45):37377-82.
134. Conte A, Pellegrini S, Tagliazucchi D. Effect of resveratrol and catechin on PC12 tyrosine kinase activities and their synergistic protection from beta-amyloid toxicity. *Drugs Exp Clin Res*. 2003;29(5-6):243-55.
135. Savaskan E, Olivieri G, Meier F, et al. Red wine ingredient resveratrol protects from beta-amyloid neurotoxicity. *Gerontology*. 2003 Nov;49(6):380-3.
136. Available at: [http://www.journalsonline.tandf.co.uk/\(rie3sl55ebw3ppe02kigd145\)/app/home/contribution.asp?referrer=parent&backto=issue,3,9;journal,11,35;linkingpublicationresults,1:100646,1](http://www.journalsonline.tandf.co.uk/(rie3sl55ebw3ppe02kigd145)/app/home/contribution.asp?referrer=parent&backto=issue,3,9;journal,11,35;linkingpublicationresults,1:100646,1). Accessed June 22, 2006.
137. Gazdikova K, Gvozdjakova A, Kucharska J, et al. Effect of coenzyme Q10 in patients with kidney diseases. *Cas Lek Cesk*. 2001 May 24;140(10):307-10.
138. Available at: <http://cancerweb.ncl.ac.uk/cancernet/600916.html>. Accessed June 19, 2006.
139. Aydogdu N, Atmaca G, Yalcin O, et al. Protective effects of L-carnitine on myoglobinuric acute renal failure in rats. *Clin Exp Pharmacol Physiol*. 2006 Jan;33(1-2):119-24.
140. Savica V, Santoro D, Mazzaglia G, et al. L-carnitine infusions may suppress serum C-reactive protein and improve nutritional status in maintenance hemodialysis patients. *J Ren Nutr*. 2005 Apr;15(2):225-30.
141. Kazmi WH, Obrador GT, Sternberg M, et al. Carnitine therapy is associated with decreased hospital utilization among hemodialysis patients. *Am J Nephrol*. 2005 Mar;25(2):106-15.
142. Bellinghieri G, Santoro D, Calvani M, Savica V. Role of carnitine in modulating acute-phase protein synthesis in hemodialysis patients. *J Ren Nutr*. 2005 Jan;15(1):13-7.
143. Grazi G, Meriggioli M, Donati G. Can the treatment with L-carnitine improve the inflammation in chronic hemodialysis patients? *G Ital Nefrol*. 2004 Nov;21 Suppl 30:S204-7.
144. Sener G, Sehirli O, Ipci Y, et al. Protective effects of taurine against nicotine-induced oxidative damage of rat urinary bladder and kidney. *Pharmacology*. 2005 Apr;74(1):37-44.
145. Bosgelmez II, Guvendik G. Effects of taurine on oxidative stress parameters and chromium levels altered by acute hexavalent chromium exposure in mice kidney tissue. *Biol Trace Elem Res*. 2004;102(1-3):209-25.
146. Mozaffari MS, Miyata N, Schaffer SW. Effects of taurine and enalapril on kidney function of the hypertensive glucose-intolerant rat. *Am J Hypertens*. 2003 Aug;16(8):673-80.
147. Verzola D, Bertolotto MB, Villaggio B, et al. Taurine prevents apoptosis induced by high ambient glucose in human tubule renal cells. *J Investig Med*. 2002 Nov;50(6):443-51.

148. Iqbal M, Sharma SD, Okazaki Y, Fujisawa M, Okada S. Dietary supplementation of curcumin enhances antioxidant and phase II metabolizing enzymes in ddY male mice: possible role in protection against chemical carcinogenesis and toxicity. *Pharmacol Toxicol.* 2003 Jan;92(1):33-8.

149. Jiang MC, Yang-Yen HF, Yen JJ, Lin JK. Curcumin induces apoptosis in immortalized NIH 3T3 and malignant cancer cell lines. *Nutr Cancer.* 1996;26(1):111-20.

150. Tirkey N, Kaur G, Vij G, Chopra K. Curcumin, a diferuloylmethane, attenuates cyclosporine-induced renal dysfunction and oxidative stress in rat kidneys. *BMC Pharmacol.* 2005;515.

151. Gaedeke J, Noble NA, Border WA. Curcumin blocks fibrosis in anti-Thy 1 glomerulonephritis through up-regulation of heme oxygenase 1. *Kidney Int.* 2005 Nov;68(5):2042-9.

152. Ali BH, Al-Wabel N, Mahmoud O, Mousa HM, Hashad M. Curcumin has a palliative action on gentamicin-induced nephrotoxicity in rats. *Fundam Clin Pharmacol.* 2005 Aug;19(4):473-7.

153. Okazaki Y, Iqbal M, Okada S. Suppressive effects of dietary curcumin on the increased activity of renal ornithine decarboxylase in mice treated with a renal carcinogen, ferric nitrilotriacetate. *Biochim Biophys Acta.* 2005 Jun 10;1740(3):357-66.

154. Available at: <http://www.cerefolin.com/SuperiorHCYEffect>. Accessed June 19, 2006.

All Contents Copyright © 1995-2009 Life Extension Foundation All rights reserved.

LifeExtension[®]

These statements have not been evaluated by the FDA. These products are not intended to diagnose, treat, cure or prevent any disease. The information provided on this site is for informational purposes only and is not intended as a substitute for advice from your physician or other health care professional or any information contained on or in any product label or packaging. You should not use the information on this site for diagnosis or treatment of any health problem or for prescription of any medication or other treatment. You should consult with a healthcare professional before starting any diet, exercise or supplementation program, before taking any medication, or if you have or suspect you might have a health problem. You should not stop taking any medication without first consulting your physician.