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AS WE SEE IT

Doctors Overlook Novel Methods to Prevent Heart Attack



Two recent studies published in the *New England Journal of Medicine* validate the role that C-reactive protein plays in increasing cardiovascular disease risk.^{1,2}

C-reactive protein is a blood marker that reveals the level of inflammatory reactions in the body. Chronic inflammation is a major cause of atherosclerosis.³ Published studies have demonstrated that elevated C-reactive protein is a greater risk factor than high cholesterol in predicting heart attack and stroke.⁴⁻⁹

Life Extension members were warned about the dangers of C-reactive protein long ago, and they take steps to keep their blood levels of this inflammatory marker as low as possible.



by William Faloon

The findings reported in the *New England Journal of Medicine* show that people who attained the lowest levels of C-reactive protein and LDL (low-density lipoprotein) had significantly reduced rates of heart attack. The studies also showed that reducing C-reactive protein (CRP) levels alone cuts heart attack risk and slows the progression of atherosclerosis. The authors of one of the studies recommend basing heart disease treatment on the results of blood tests that measure CRP as well as LDL levels.

In these *New England Journal of Medicine* studies, researchers administered moderate to high doses of “statin” drugs to heart disease patients in order to lower their LDL and CRP levels. We at Life Extension are not averse to the use of low-dose statin drugs for those who cannot achieve optimal LDL and CRP blood ranges using natural approaches. We take issue, however, with the blanket recommendation that virtually everyone could benefit from statin drug therapy. Statin drugs have proven side effects, and there are safer approaches that people can try first to attain the same benefits of statins.

Some doctors tell their patients to eat anything they want as long as they take their statin drug. This is bad medicine, and patients who rely on this kind of advice face severe health consequences.

HOW DIET AFFECTS C-REACTIVE PROTEIN LEVELS

An increasing body of evidence demonstrates that eating too much saturated fat or high-glycemic carbohydrates increases C-reactive protein.¹⁰

One study showed a 39% decrease in CRP levels after only eight weeks of consuming a diet low in saturated fat and cholesterol. The study participants also saw reductions in their LDL, total cholesterol, body weight, and arterial stiffness after eight weeks.¹¹



Other studies show that eating high-glycemic foods increases CRP by promoting excess production of a pro-inflammatory cytokine called interleukin-6 (IL-6).¹² CRP is produced in the liver primarily by excess levels of IL-6. One study showed a 28% reduction in CRP levels when women consumed a whole-food vegan diet rich in soluble fiber. One researcher suggested that it might be possible to achieve meaningful reductions in CRP by avoiding high-glycemic foods and ingesting soluble fiber at mealtime.¹³

In the September 2004 issue of *Life Extension*, we published an extensive article (“Novel Fiber Limits Sugar Absorption”) showing that consuming soluble fiber before a meal slows the absorption of high-glycemic foods and lowers post-meal blood glucose and insulin levels. Excess insulin is a significant cause of elevated CRP.^{13,14-19}

Perhaps the most notable study compared the effects of three different dietary regimens on LDL and CRP blood levels. Group 1 consumed a diet very low in saturated fat, which included whole-grain fiber and dairy protein. Group 2 consumed the same low-fat

diet plus a statin drug. Group 3 ingested cholesterol-lowering foods such as almonds, soy protein, plant sterols, and soluble fibers.

The striking results showed that the cholesterol-lowering foods worked almost as well as the very low-fat diet plus statin drug therapy. After 30 days, those who ate the cholesterol-lowering foods showed a 28.2% reduction in CRP and a 28.6% reduction in LDL. Those who received the statin drug and consumed a very low-fat diet showed a 33.3% reduction in CRP and a 30.9% reduction in LDL. (Group 1, which consumed a very low-fat diet only, saw a mere 10% reduction in CRP and 8% reduction in LDL.)²⁰

Few people can follow a rigorous low-fat diet. What this study revealed is that functional foods—such as almonds, soy protein, fiber, and plant sterols—are almost as effective as a very low-fat diet plus a statin drug in reducing markers of cardiovascular risk. It is easier and safer to consume functional foods than to follow a very low-fat diet and take a statin drug.

Although published in the *Journal of the American Medical Association*, this impressive study received scant media attention. Since drug companies have no interest in the public finding out that functional foods are a more efficient way than drugs to lower LDL and CRP, there was no public relations campaign to announce these findings in the media.²⁰

For doctors to not counsel patients about healthy diet but instead prescribe high-dose statin drug therapy is scientifically inappropriate. What is apparent from the recent *New England Journal of Medicine* studies, however, is that testing one's blood to ascertain LDL and CRP levels is more important than ever. The *New England Journal of Medicine* studies clearly show that reduced heart attack risk directly correlates with therapeutic lowering of CRP and LDL.

CARNITINE SUPPLEMENTS LOWER CRP

A number of dietary supplements are known to lower C-reactive protein, but new studies indicate that the amino acid L-carnitine may also be effective. One study evaluated patients undergoing kidney dialysis, which causes increased CRP levels. Treatment using about 1500 mg of L-carnitine only three times a week resulted in a reduction of CRP levels with a corresponding improvement in other indicators of patient health. Most Life Extension members take around 1500 mg of carnitine every day.²¹

Another study revealed that in addition to lowering CRP levels in dialysis patients, supplemental L-carnitine also resulted in improved body mass index, most likely the result of reducing insulin resistance. The authors concluded that supplemental L-carnitine both suppresses inflammatory reactions and improves metabolic (glucose control) status.²²

ELEVATED CRP MAY INCREASE ALZHEIMER'S RISK

While most studies have focused on the cardiovascular dangers of C-reactive protein, it is important to remember that CRP can be a blood marker of a chronic inflammatory state in the body. Chronic inflammation is an underlying cause of many age-related diseases. Recent studies indicate that high CRP may increase one's risk of Alzheimer's disease, in addition to the risk of dementia induced by blood vessel disease in the brain.³⁵

FISH OIL MAY NOT LOWER CRP

Fish oil is one of the better-documented nutrients for preventing heart attacks. A study published by the American Heart Association showed that people who consumed a low-dose fish oil supplement (1000 mg a day) were 45% less likely to die from a heart-related disease over a 3.5-year period.²⁴

Previous studies have indicated that fish oil reduces C-reactive protein. A recent study showed that women with high levels of EPA and DHA fatty acids in their blood had 56% lower CRP.²⁵ Other recent studies show reductions in CRP in response to supplemental fish oil intake.^{26,27}

In response to positive evidence that fish oil reduces inflammatory blood markers,²⁸ researchers initiated studies to ascertain exactly how effective fish oil supplements are in lowering CRP. Some of these studies showed that fish oil does not lower CRP. One study showed no CRP reduction in response to moderate intake of fish oil (1.35 grams of EPA/DHA).²⁹ Another study found that 1.5 grams of EPA/DHA did not lower CRP.³⁰ Most Life Extension members take 2.4 grams of EPA/DHA that also contains sesame lignans to augment its anti-inflammatory effect.

A study of type II diabetic patients showed that 4 grams of EPA/DHA significantly reduced markers of oxidative stress but did not lower CRP compared to placebo. This study's potential flaw is that the placebo was olive oil, which has its own CRP-lowering effects.³¹ The fact that fish oil did not lower CRP compared to olive oil may not be that significant.³²

PERIODONTAL DISEASE INCREASES CRP

Published studies show that people with destructive gum disease almost double their

risk of heart attack. These studies indicate that in response to periodontal therapy, C-reactive protein levels decline dramatically. A recent study emphasized the importance of oral hygiene as a way to "prevent the onset or progression of cardiovascular disease."²³ Instead of recommending periodontal therapy to patients, many cardiologists now prescribe higher doses of statin drugs to lower CRP.

Another study compared the effects of varying doses of fish oil to an olive oil placebo. The results showed no effect on CRP levels in the fish oil group, but by again using olive oil as the placebo, these findings are not conclusive because the olive oil may have also lowered CRP.³³

Contradicting these recent negative studies is a recent positive study showing that fish oil reduced CRP levels when safflower oil was used as a placebo. Unlike olive oil, safflower oil has not shown CRP-lowering properties and is therefore a more appropriate placebo.³⁴

Fish oil has documented anti-inflammatory properties, but it may not be the most effective way to lower CRP.

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HOW EFFECTIVE IS VITAMIN E?

If you were to ask a nutritionist which supplement most effectively lowers C-reactive protein, the most likely answer would be vitamin E. Numerous studies show a significant CRP-lowering effect in response to supplemental vitamin E.^{36,37} A recent study of baboons showed that alpha tocopherol vitamin E reduced CRP by 52%. When coenzyme Q10 was added to the vitamin E supplementation program, CRP was reduced by 70% compared to baseline.³⁸

Cigarette smoking causes a significant increase in CRP. In a recent study of smokers with established heart disease, 400 IU of alpha tocopherol reduced CRP by an impressive 57%.³⁹

Those with kidney disease undergoing dialysis have high CRP levels. In a study of patients with end-stage kidney disease, 400 IU of alpha tocopherol did not lower CRP levels. This study, however, revealed that in response to alpha tocopherol supplementation, gamma tocopherol levels in the body declined by 61%.⁴⁰ This finding is significant because of evidence that gamma tocopherol is the preferred form of vitamin E to reduce inflammatory processes.⁴¹

In a related study, administration of a gamma tocopherol supplement to dialysis patients resulted in a 52% reduction in C-reactive protein, helping to confirm the critical importance of the gamma form of vitamin E.⁴⁰

A large body of published research indicates that vitamin E, in either alpha or gamma form, reduces CRP in both healthy individuals and those with serious disease.⁴²



FIBER AND CRP LEVELS

As noted earlier, what you eat has a lot to do with your CRP level. Ingesting soluble fiber before you eat diminishes the post-meal spike of excess glucose and insulin in the blood.

In a recent study conducted under the auspices of the Centers for Disease Control and Prevention, 3,920 participants who participated in the National Health and Nutrition Examination Survey were evaluated to ascertain dietary fiber intake and blood CRP levels.⁴⁴

The CRP level of study subjects who ingested the most dietary fiber was 41% lower than the level of those who ate the least fiber. The doctors who conducted this study concluded:

“Our findings indicate that fiber intake is independently associated with serum CRP concentration and support the recommendation of a diet with a high fiber content.”

A higher intake of dietary fiber may decrease the risk of developing cardiovascular disease. Studies have documented that consuming more fiber safely lowers CRP. Yet cardiologists are overlooking the multiple beneficial effects of fiber in not only lowering CRP, but also reducing excess blood glucose and insulin. All of these factors—CRP, glucose, and insulin—contribute to the atherosclerosis process.

DEPRESSION INCREASES CRP LEVELS

Research has linked depression with an increased incidence of heart attack. A new study of 6,914 men and women showed that a history of major depression is associated with a 39% increase in C-reactive protein. Among men who had an episode of major depression within the previous year, CRP levels were three times higher than in men who had not suffered from depression. The authors concluded:

“Major depression is strongly associated with increased levels of CRP among men and could help explain the increased risk of cardiovascular disease associated with depression in men.”⁴³

WHAT LEVEL OF C-REACTIVE PROTEIN IS OPTIMAL?

The standard reference range for C-reactive protein (CRP) is 0-3.00 milligrams per liter (mg/L) of blood. The standard reference ranges indicate that CRP under 1.00 mg/L is ideal, between 1.00 and 3.00 mg/L is average, and over 3.00 mg/L is cause for concern.⁴⁵



As has been the case for many years, we at Life Extension vehemently disagree with today's standard reference ranges. It is our contention—based on published scientific research—that CRP should be under 0.55 mg/L in men and under 1.50 mg/L in women.

If you were a man relying on your doctor to interpret your blood test results, he would view a CRP level of 2.00 mg/L as being “average.” That would put you at “average” risk of having a heart attack, which happens to be a leading cause of death. Why anyone would accept an “average” risk of having a heart attack is beyond our comprehension.

Life Extension has been consistently ahead of conventional medicine in determining optimal blood marker levels. Since our inception, we have stated that ideal levels of glucose and LDL are under 100 mg/dL of blood. Only recently were reference ranges for glucose lowered from 109-124 to less than 100 mg/dL. Several years ago, doctors announced that LDL should ideally be less than 100 mg/dL instead of the previously accepted range of up to 130 mg/dL.

MAINSTREAM MEDICINE'S MEDIOCRE OBJECTIVES

The two studies published in the *New England Journal of Medicine* received a lot of publicity because they showed that statin drugs cut heart attack risk by lowering CRP.

The percentage of CRP reduction, however, was not that significant. In one study that evaluated the effects of moderate- to high-dose statin drug therapy, CRP was reduced on average from 2.9 to 2.3 mg/L—a 21% reduction. The other *New England Journal of Medicine* study observed heart attack risk reduction when CRP fell below 2.00 mg/L and 1.00 mg/L.^{1,2}

We at Life Extension are not impressed by these modest reductions in CRP, yet they are considered a breakthrough by conventional medicine's mediocre standards.

When you consider that people with a high dietary intake of fiber have 41% lower CRP levels, that supplementation with alpha or gamma tocopherol was shown to lower CRP by around 50%, and that merely eating functional foods such as almonds and soy protein reduces CRP by 28%, the effect of very high-dose statin drugs in reducing average CRP levels by 21% is not remarkable.

What's striking is the reduction in heart attack risk and the slowing of coronary atherosclerosis in patients receiving the statin drugs. We believe that some of these benefits are attributable to the effects of statin drugs in improving the health of the arterial wall (endothelial function), a mechanism that was not discussed in the press reports. These same effects, however, have also been demonstrated in response to supplementation with folic acid,⁴⁶⁻⁵¹ fish oil,⁵²⁻⁵⁴ vitamin C,⁵⁵⁻⁵⁹ and lipoic acid.⁶⁰⁻⁶⁴

SOME COMMON-SENSE APPROACHES

For those with coronary atherosclerosis who do not respond to natural approaches, statin drug therapy may be considered. For a statin drug like Lipitor®, ask your doctor about taking 10 mg every other day. Higher doses should be considered only when all else fails.

The subjects in the *New England Journal of Medicine* studies were given daily doses of 80 mg of Lipitor® (a very high dose) or 40 mg of Pravachol® (a moderate dose). The best results occurred when blood tests revealed LDL levels under 70 mg/dL and CRP under 1.00 mg/L. To achieve these results, the subjects used a daily dose of up to 80 mg of Lipitor®. In some cases, the more moderate dose of 40 mg of Pravachol® achieved the same optimal blood results. The researchers emphasized that the favorable clinical results were based solely on the blood test numbers—that is, it did not matter which drug (Lipitor® or Pravachol®) was used. Those with the lowest LDL and CRP had the fewest heart attacks and slower progression of coronary atherosclerosis.

The problem with using 80 mg of Lipitor® daily is side effects. Some of the toxicities associated with high-dose intake of statin drugs are well known, while the long-term effects are unknown.

If a cardiac patient wishes to achieve LDL levels below 70 mg/dL, it might be safer to use a lower dose of Lipitor® combined with a diet-modification program. This program would include: eating cholesterol-lowering functional foods such as almonds and soy protein; consuming soluble fiber before each meal; avoiding trans fatty acids, saturated fats, and high-glycemic carbohydrates; and supplementing with alpha and gamma tocopherol and acetyl-L-carnitine, along with fish oil, folic acid, vitamin C, and lipoic acid. These nutrients are known to help suppress triglycerides, maintain healthier endothelial function, and suppress CRP. Using natural supplements like Sytrinol™ could further reduce the statin drug dose needed to lower LDL levels.

THE STATIN DRUG CONTROVERSY

There has been a longstanding dispute between mainstream and alternative medicine regarding the safety and efficacy of statin

drugs. We at Life Extension have taken a balanced approach in our reporting, emphasizing both the pros and cons of statin drug therapy.

In the November 2004 issue of *Life Extension*, an article entitled "Cholesterol & Statin Drugs: Separating Hype from Reality," authored by William Davis, MD, presented the facts about the benefits of statins, along with data showing that these drugs are often over-prescribed.⁶⁶

One of the problems we have identified when evaluating our members' blood test results is that cholesterol levels are often reduced too much in response to statin drug therapy. It is our position that the ideal cholesterol blood level is 180-200 mg/dL and that levels below 160 mg/dL are particularly dangerous. Cholesterol is required for the natural synthesis of hormones,^{67,68} for blood vessel wall maintenance,⁶⁹ and for maintaining proper cell membrane structure and function.⁷⁰ Driving cholesterol to abnormally low levels can wreak havoc throughout the body.

The dose of statin drugs prescribed by most doctors often results in cholesterol readings far below 160 mg/dL. The obvious solution to this problem is to take a lower dose of the statin drug. We have found that cutting the dose of a statin drug in half and even by three-quarters maintains LDL under 100 mg/dL and total cholesterol under 200 mg/dL.



How dangerous is too-low cholesterol? A huge study followed 350,977 middle-aged men for an average of 12 years. Those whose total cholesterol levels were under 160 mg/dL doubled their risk of brain hemorrhage and significantly increased their risk of death from cancers of the liver and pancreas, digestive diseases (particularly hepatic cirrhosis), suicide, and alcohol dependence syndrome. In addition, men with total cholesterol under 160 mg/dL had increased risks of cancers of the lung, lymphatic, and blood (leukemia) systems, and chronic obstructive pulmonary disease.⁷¹

A study of 11,563 men showed that over a five-year period, men whose cholesterol levels were below 160 mg/dL had a 2.27-fold increase in mortality from non-cardiac deaths and the same rate of death for heart attack compared to men with higher cholesterol levels.⁷²

Numerous studies indicate that those with cholesterol levels below 160 mg/dL suffer severe health consequences, with mental depression and suicide being particularly troublesome. Since cholesterol is the precursor to "feel good" hormones like testosterone and estrogen, some scientists believe that reducing cholesterol to too low a level can have a significantly negative impact on one's mental health.⁷³⁻⁷⁹

Doctors are prescribing higher-dose statin drugs for the purpose of preventing heart attacks without considering that these same drugs may be lowering their patients' cholesterol levels too much. We at Life Extension have long advocated safer approaches for maintaining vascular health that may accomplish better results without side effects. While drug company public relations firms and the media heavily tout the statin drugs, Life Extension members learn the facts that underlie the headlines.

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WHAT IS YOUR CRP LEVEL?

There are numerous reasons why a chronic inflammatory state can take hold of your body. The good news is that inflammation can be measured by an inexpensive, high-sensitivity C-reactive protein blood test, and correctable actions can be taken if CRP levels are too high. Too often, inflammatory reactions silently inflict destruction throughout the body until a major event like a heart attack, kidney failure, stroke, or Alzheimer's disease manifests.

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. The impact that these blood tests have had in preventing future disease and premature death is incalculable.

The problem members used to encounter was that their doctors refused to prescribe blood tests for important markers like homocysteine, DHEA, and C-reactive protein. The retail price for these tests was also cost prohibitive. In 1996, Life Extension resolved this problem by offering blood tests at discounted prices directly to its members.

Once a year, we reduce our everyday low prices even more to Life Extension members. These low prices enable members to obtain extensive blood test panels for a fraction of the price charged by doctors' offices or commercial laboratories.

I have personally derived enormous benefits from having my blood regularly tested. My familial predisposition results in very high levels of artery-clogging homocysteine. By having regular blood tests, I have been able to adjust my intake of vitamin B6 (to around 1000 mg a day), along with folic acid, vitamin B12, and TMG (trimethylglycine), to keep homocysteine levels in check. Had I not tested my blood, I would have assumed that my vitamin supplements were adequately suppressing homocysteine.

I know that members take supplements like Sytrinol™ to maintain healthy levels of LDL, fish oil to reduce triglycerides, and a variety of nutrients to keep C-reactive protein as low as possible. It is critical that the effects of these supplements and any drugs you may be taking be measured not only to verify that they are producing the desired results, but also—in the case of prescription drugs—to guard against adverse side effects. An annual blood test is the most effective way to monitor your overall health.

In this month's issue, we describe the most important blood tests you should consider. Whether using your own doctor 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



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