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Cardiovascular Disease Risk Factors – Part VIII C-Reactive Protein

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The American Heart Association and the American College of Cardiology identifies both primary risk factors for heart disease and “predisposing” factors.

Predisposing risk factors

These are conditions which worsen the independent risk factors, but which are not in and of themselves presently identified as risk factors for cardiovascular heart disease. In the future and perhaps in the new future some of them will move to either the conditional or the major/independent categories of cardiovascular risk. The factors which are predisposing are:

- Elevated serum triglycerides
- Small LDL particles
- Elevated serum homocysteine
- Elevated serum lipoprotein(a)
- Prothrombotic factors (eg, fibrinogen)
- Inflammatory markers (eg, C-reactive protein)

“Inflammation” is the process by which the body responds to injury. Laboratory evidence and findings at autopsy studies suggest that the inflammatory process plays an important part in atherosclerosis, which is the process in which fatty deposits build up in the lining of the arteries. We call this “hardening of the arteries.”

C-reactive protein (CRP) is a protein in the body whose level increases when there is inflammation of the blood vessels. Researchers have found that blood levels of CRP are elevated many years before a first heart attack or stroke. Overall, researchers have found that men with the highest C-Reactive protein, compared to men with lower levels of the protein:

“Have a threefold increase in their risk for heart attack - Have a twofold increase in their risk for stroke. These risks are independent of other risk factors, including high blood cholesterol, smoking, high blood pressure, obesity and diabetes. The six to eight year advance warning is enough time for someone to begin an aggressive prevention program.”

What causes low-grade inflammation in blood vessels?

No one knows for sure, but new findings are consistent with the hypothesis that an infection, possibly caused by a virus or bacteria, might contribute to or even cause atherosclerosis. Possible infectious bacteria include *Chlamydia pneumoniae* and *Helicobacter pylori*. Possible viral agents include herpes simplex and cytomegalovirus.

Someday, antimicrobial or antiviral therapies may become part of the prevention of heart attacks.

CRP After Acute Myocardial Infarction

After an acute myocardial infarction (AMI), acute phase inflammatory markers appear to affect prognosis. C-reactive protein values are known to increase in acute coronary syndromes, such as unstable angina and myocardial infarction, and are associated with adverse outcomes. Researchers have evaluated the prognostic significance of C-reactive protein values in patients considered to be at low risk for long-term adverse outcomes after a first, uncomplicated AMI and normal left ventricular function.

In one important trial, venous blood samples were analyzed for C-reactive protein at a mean time of eight hours after the onset of symptoms in 64 patients with AMI. The diagnosis was confirmed by elevated creatine kinase-MB values. Follow-up testing included echocardiography and exercise stress tests (seven to eight days after the event) and coronary angiography (approximately one month after the event). Follow-up examination was conducted every three months after discharge for the next year.

All patients were treated with nitrates and aspirin, and many received beta blockers with or without angiotensin-converting enzyme (ACE) inhibitors. No patient had an ejection fraction of less than 45 percent. Angiography identified the infarct-related vessel in all patients, and no patient had collateral blood vessels.

Patients who died during the follow-up period had significantly higher mean C-reactive protein values. Patients with a C-reactive protein value of more than 2.55 mg per dL had a cardiac event incidence of 56 percent, including cardiac death, unstable angina and recurrent myocardial infarction. C-reactive protein values assayed at hospital admission can predict the risk of long-term ischemic events in patients with a first AMI who are otherwise considered to be at low risk. These assays can contribute to more complete risk stratification in these patients.

Predicting Risk of Heart Attack with CRP

Measuring C-reactive protein with a high sensitivity test adds to the predictive value of screening blood samples for both total and HDL (good) cholesterol levels. Thus C-reactive protein testing may improve doctors' ability to predict heart disease risk among women and men.

Measuring C-reactive protein with high-sensitivity test procedures seems to allow detection of how much underlying atherosclerosis a patient has and thus predict the risk of future heart attack and stroke events.

In a study, which measured C-reactive protein levels in blood samples obtained from participants in the Women's Health Study, an ongoing evaluation of 39,876 healthy, post-menopausal American women, women with the highest levels of C-reactive protein had a

five-fold increase in the risk of developing any cardiovascular disease and a seven-fold increase in risk of having a heart attack or a stroke, when compared to those with the lowest levels of C-reactive protein.

Levels of C-reactive protein predicted these events even among apparently low-risk women, such as those who did not smoke, had no evidence of high cholesterol and no family history of heart disease. These data confirm that increased levels of C-reactive protein are a strong marker of risk not only in middle-aged men, but also in healthy women.

Blood Tests for C-Reactive Protein

This blood test is used as an indicator of acute inflammation. C-reactive protein is produced by the liver during periods of inflammation. C-reactive protein plays a role in stimulating the body's complement system. Normally C-reactive protein should be negative in the bloodstream. Conditions which can cause a positive C-reactive protein include: rheumatoid arthritis, lupus, pneumococcal pneumonia, rheumatic fever, cancer, tuberculosis, and myocardial infarction. A positive C-reactive protein may also be seen in the later half of pregnancy and in some who are taking birth control pills.

However, it must be remembered that only the high sensitivity C-Reactive Protein values have predictive value as to cardiovascular and/or stroke risk assessment.

Conditions which elevate CRP and Cardiovascular risk

Increased levels of C-reactive protein are associated with:

- weight gain,
- obesity, and
- use of hormone replacement therapy (HRT) in postmenopausal women.

Both overweight (body mass index [BMI], between 25-29.9) and obese (BMI over 30) persons were more likely to have elevated CRP levels than their normal-weight counterparts (BMI, less than 25). Higher BMI is associated with higher CRP concentrations, even among young adults aged 17 to 39 years. These findings suggest a state of low-grade systemic inflammation in overweight and obese persons.

Excessive use of alcohol causes increased CPR, as does smoking and a sedentary life style.

What To Do If You Have Elevated C-Reactive Protein

Statins

Statins, a class of drugs named HMG-CoA reductase (lipid lower agents, such as Pravastatin, Lipitor, Zocor, etc.), in long-term therapies appear to result in significant reduction of CRP levels. A study which did baseline analysis and five-year follow-up blood samples from

the Cholesterol and Recurrent Events (CARE) suggested that it may be possible to alter the CRP and thus decrease the inflammation in the lining of arteries and thereby improve the function of the lining of the arteries.

The mechanism for this improvement in the CPR and the decreasing of the cardiovascular risk may be an improvement in what is called "endothelium dysfunction." The "endothelium" is the lining of the artery. The endothelium has a complex function in maintaining the health of the blood vessels. The function of the endothelium is adversely affected by elevated blood sugar, elevated circulating fats in the blood and by infections. Decreases in the blood cholesterol and triglycerides have shown improvement in the endothelium function in less than two weeks with improvement in blood flow in the artery. The CARE trial was a secondary prevention trial of cardiovascular disease in 4159 patients with a history of myocardial infarction who had total cholesterol <240 mg/dL and LDL cholesterol between 115 and 175 mg/dL.

Aspirin

Aspirin decreases the risk of blood clots in the arteries and also has anti-inflammatory properties. The Consortium for Physician Performance Improvement, made up of the AMA, CMS, National Academy of Medicine and the heads of the Medical and Surgical Specialty Societies, has published performance standards for the management of Chronic Stable Angina. Among those standards is that every person who has angina (heart pain) should be on an anti-platelet therapy similar to aspirin. In fact, unless a person has a bleeding tendency, or is on Coumadin, almost everyone would benefit from a low-dose aspirin a day.

Because of its anti-clotting and anti-inflammatory properties aspirin may have a benefit in decreasing inflammation of the arteries and therefore improving the CPR levels.

Antibiotics

Some researchers believe you should take antibiotics to inhibit inflammation that can lead to heart disease. I remember the first time I heard that someone was treating ulcers with antibiotics. I thought it was a silly idea, but now it is standard practice. We are not "there yet," but the day may come when patients at high risk for coronary artery disease and who have a high CPR will be placed on prophylactic antibiotics.

Enhancing the Immune System

The best natural approach to combat C-reactive protein is to take immune-boosting supplements. Some that are often recommended are:

Coenzyme Q10. This nutrient is one of the best there is for promoting the immune system. Take 100 to 200 milligrams daily or 2 to 4 softgels. Beta 1/3, 1/6 glucan. This yeast-based nutrient promotes a healthy immune system by scavenging for free radicals, which can wreak all kinds of havoc with your health, including your heart. It promotes the killer

activity of white blood cells. There's no toxicity or side effects with this nutrient. Take 10 to 20 mg daily. Ginger root/ginger tea. Ginger promotes the inflammatory response and it's a great substitute for aspirin, which many people can't tolerate. Fish oil. Promotes thinning of the blood. Exercise and diet

High sensitivity C-reactive protein (hs-CRP) can be effectively reduced by non-pharmacologic therapy using a structured program of exercise training and diet. In a recent study, researchers sought to determine whether a structured program involving a low-fat, Mediterranean diet and a supervised, three-times weekly exercise program for three months could have a positive effect on hs-CRP values.

The study assessed hs-CRP and traditional cardiac risk factors in 65 coronary artery disease (CAD) patients following PTCA and MI. The patients, who had a mean age of 64, plus or minus 10 years, were measured at baseline and after completion of three months of Phase II cardiac rehabilitation and exercise training. Values of hs-CRP dropped 31 percent after the three months - from 4.2 mg/L (5th quintile of CAD risk) at baseline to 2.9 mg/L (4th quintile of CAD risk) ($p < 0.004$), the researchers found.

Noting that the changes in hs-CRP values occurred independent of lipid modulation, the researchers concluded that an approach involving low fat diet and progressive exercise training can augment pharmacologic strategies in altering inflammatory markers in CAD.

Conclusions:

The predictive value of CRP for acute MI and/or stroke is independent of traditional cardiovascular risk factors.

CPR appears to offer a prognostic advantage over measurement of lipids alone. Clinical trials suggest that the increased risk associated with inflammation may be modified with certain preventive therapies.

American Heart Association Recommendations

Regardless of one's "inflammatory risk profile," cardiologists recommend these steps to all patients and the general public for achieving and maintaining a healthy heart:

1. Stop smoking and avoid other people's tobacco smoke
2. Keep your blood pressure in check
3. Eat a healthy diet low in saturated fat, cholesterol and sodium (salt)
4. Maintain an active lifestyle and a healthy weight
5. Manage diabetes, if you have it

There has never been a time in human history where your choices and your personal decisions can be shown to have such positive or negative affects on your future well being.

Remember, it is your life and it is your health.