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## **Cardiometabolic Risk Syndrome**

### **Part VIII C-Reactive Protein**

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The cardiometabolic syndrome is principally characterized by the liver, the muscles and the fat tissue in the body being unresponsive, or resistant to the effects of insulin. There are a number of inflammatory markers which are associated with the chronic, low-grade inflammation of the cardiometabolic risk syndrome; some of them are:

- C-Reactive Protein (CRP)
- Fibrinogen
- Ferritin
- Uric Acid
- White Blood Cells
- Plasminogen Activator Inhibitor I
- Homocystiene

This chronic low-grade inflammation results in a number of abnormalities in the functioning and the structure of the blood vessels in the body, including:

- Endothelial dysfunction
- Imbalance of the equilibrium between the blood clotting and the clots being broken down.
- Atherosclerosis with the development of plaques in the arteries and particularly the unstable plaques which result in myocardial infarctions and strokes.

The cardiometabolic syndrome can be present without obesity particularly in Asian populations but in Western society and particularly the United States, the syndrome is most often associated with obesity. As a result, another important aspect of the cardiometabolic syndrome is the production of adipocytokines such as:

- TNF Alpha
- IL-6
- Dozens of others

### **Best studied and understood of the inflammatory markers: C-reactive protein**

"Inflammation" is one of the processes by which the body responds to injury or infection. This response is called an acute phase reaction and is the process whereby the body marshals the substances necessary to ward off an infection or to respond to an injury. While the protective aspects of inflammation are beneficial, there are also detrimental aspects of the inflammatory response, particularly when it goes on for a long time.

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 an acute phase reactant, a protein, in the body whose level increases when there is inflammation in the lining of the blood vessels. Blood levels of CRP are elevated many years before a first heart attack or stroke. 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
- diabetes

The good news is that the six to eight year advance warning which elevated C-reactive protein provides is enough time to begin an aggressive prevention program.

### **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.

Patients who died during the follow-up of an AMI 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.

### **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 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.

## **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 and 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
- myocardial infarction

A positive C-reactive protein may also be seen in the latter 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], 25-29.9) and obese, BMI >30 ) persons were more likely to have

elevated CRP levels than their normal-weight counterparts (BMI, <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.

Three modifiable behaviors cause increased C-reactive protein:

- Excessive use of alcohol
- Smoking
- A sedentary life style

## **What To Do If You Have Elevated C-Reactive Protein**

### ***Statins***

Statins, a class of lipid lower agents, such as Pravacol, Lipitor, Crestor and Zocor, 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." (See *The Examiner* January 4, 2007 or see [www.jameslhollymd.com](http://www.jameslhollymd.com) Life Your Health Cardiometabolic Risk Syndrome Part IV: Endothelial Dysfunction.)

### ***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. (See *The Examiner* January 25, 2007 or see [www.jameslhollymd.com](http://www.jameslhollymd.com) Your Life Your Health Cardiometabolic Risk Syndrome Part VII: Inflammation)

### **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.
- 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 trails 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.