C-reactive protein is a special type of protein produced by the liver that is only present during episodes of acute inflammation. [Current research indicates the presence of CRP in chronic low-level inflammatory conditions like cardiovascular disease] The most important role of CRP is its interaction with the complement system, which is one of the body’s immunologic defense mechanisms. C-reactive protein is produced in the liver by pro-inflammatory cytokines called interleukin-1B, interleukin-6 and tumor necrosis factor alpha.

Since the CRP is a general test, a positive CRP may indicate any of a number of things:

- Rheumatoid arthritis
- Rheumatic fever
- Cancer
- Tuberculosis
- Pneumococcal pneumonia
- Myocardial infarction
- SLE

Medline Plus Medical Encyclopedia

**We offer two tests for CRP**

*What's the difference?* CRP Quantitative is the traditional test use as a marker for various inflammations. CRP Cardiac, also called High Sensitivity CRP, is a new more sensitive test for the same substance. Both measure the same substance but the Cardiac test is like looking through a high powered microscope – you get a much better and more accurate view with the amount of the substance found being higher for the same amount of sample. This is especially useful when evaluating chronic as opposed to acute inflammation. There is risk factor reported with the Cardiac results for future MI and stroke events. In the “normal, healthy” individual CRP would be 0.0-4.9 mg/L but it has now been established that there are risk factors within the so-called normal range. If you want to know cardiac risk or you are evaluating chronic inflammation, use the cardiac CRP test.

**C-Reactive Protein (CRP), Quantitative**

**Ordering Code** 006627 **CPT Code** 86140

*From Lab Corp’s Directory Of Services…*

CRP is an acute phase reactant, which can be used as a test for inflammatory diseases, infections, and neoplastic diseases. Progressive increases correlate with increases of inflammation/injury. CRP is a more sensitive, rapidly responding indicator than ESR (Sed rate). CRP may be used to detect early postoperative wound infection and to follow therapeutic response to anti-inflammatory agents. Recent reports have indicated that a highly sensitive version of the CRP assay may be used as an additional indicator for susceptibility to cardiac disease.
CRP arises as a nonspecific response to tissue injury and inflammation.

CRP is a pentameric globulin with mobility near the gamma zone. It is an acute phase reactant, which rises rapidly, but nonspecifically in response to tissue injury and inflammation. It is particularly useful in detecting occult infections, acute appendicitis, particularly in leukemia and in postoperative patients. In uncomplicated postoperative recovery, CRP peaks on the 3rd post-op day, and returns to pre-op levels by day 7. It may also be helpful in evaluating extension or reinfarction after myocardial infarction, and in following response to therapy in rheumatic disorders. It may help to differentiate Crohn’s disease (high CRP) from ulcerative colitis (low CRP), and rheumatoid arthritis (high CRP) from uncomplicated lupus (low CRP).

**C-Reactive Protein (CRP), Cardiac**

**Ordering Code** 120766  **CPT Code** 86141

From Lab Corp’s Directory Of Services… Measurement of CRP by high sensitivity CRP assays may add to the predictive value of other markers used to assess the risk of cardiovascular and peripheral vascular disease.

Increases in CRP values are nonspecific. CRP is an indicator for a wide range of disease processes and should not be interpreted without a complete clinical history. Recent medical events resulting in tissue injury, infections or inflammation, which may cause elevated CRP levels, should also be considered when interpreting results. Serial analysis of CRP should not be used to monitor the effects of treatment.

**Relative Risk Category**

<table>
<thead>
<tr>
<th>Category</th>
<th>Average hs-CRP Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>&lt;1.0 mg/L</td>
</tr>
<tr>
<td>Average</td>
<td>1.0 mg/L - 3.0 mg/L</td>
</tr>
<tr>
<td>High</td>
<td>&gt;3.0 mg/L</td>
</tr>
</tbody>
</table>

More specific risk ranges appear on lab Reports.

**Related Tests For Inflammation Assessment**

Serum amyloid A [SAA]; fibrinogen; erythrocyte sedimentation rate (ESR), homocysteine, WBC count, serum albumin, cytokines (interleukin-6 and TNF -Tumor Necrosis Factor), histamine, monocytes, and may also include such things as liver enzymes that may indicate inflammation and makers for UTI and infection in general.

**Research Information**

**CRP Related to Arterial Calcification**

“a random sample of 321 patients from FHS (Framingham Heart Study) who underwent blood tests to measure CRP and, after stratification by CRP level, subsequently underwent electron-beam computed tomography (EBCT) to detect the presence of sub clinical coronary atherosclerosis, as measured by a coronary artery calcification (CAC) score. Researchers found, after adjusting for other risk factors, that there was a direct correlation between elevated levels of CRP and higher CAC scores (P < .01) in both men and women.”

Excerpts from: Medscape Cardiology 10/15/2002 Michelle Bridenbaker

**Numerous Studies Relate CRP to Cardiovascular Disease**

“There is a preponderance of research that has illustrated a very strong correlation between CRP and cardiovascular disease, especially when viewed concurrently with other known risk factors (ie, smoking, obesity, low HDL cholesterol, high blood pressure, and decreased physical activity).”

Excerpts from: Medscape Cardiology 10/15/2002 Michelle Bridenbaker

The addition of the measurement of C-reactive protein to screening based on lipid levels may provide an improved method of identifying women at risk for cardiovascular events.


**Cellular processes leading to atherosclerosis**

As part of the "innate defense," CRP binds to monocytes, macrophages, and neutrophils and activates the complement system cascade.
(protein-mediated immune response) that leads to the opsonization (a process that facilitates particle binding to phagocytes) of "foreign" molecules. If this occurs on the endothelial tissue of arteries, fatty deposits will remain with the macrophages in the intima (fatty streaks) of these vessels and subsequently begin the process of atherosclerosis. Excerpts from: Medscape Cardiology 10/15/2002 Michelle Bridenbaker

Comment: It may be that those with a dual elevation of CRP and monocytes are in a high-risk group since CRP binds to monocytes.

Bacterial Implications in CRP Elevations

Persistently but not transiently elevated C pneumoniae IC/IgA and hHsp60 IgA (human heat shock protein 60) antibodies, especially when present together with an elevated CRP level, predicted coronary events. Circulation. 2003 May 27;107(20):2566-70. Epub 2003 May

Atherosclerotic plaques were likened histologically to healing inflammatory lesions by Russell Ross, who proposed a "response to injury" hypothesis for their formation.

Potential causes for vascular injury include mechanical stress, smoke exposure, hypercholesterolemia, hyperhomocysteinemia, and chronic infection.

Blood levels of inflammatory markers including C-reactive protein [CRP]; serum amyloid A [SAA]; fibrinogen; plasma viscosity; erythrocyte sedimentation rate [ESR]; leukocyte count, low serum albumin and more recently cytokines (e.g., interleukin-6 [IL-6]) and soluble adhesion molecules have been associated with vascular risk.


New data connects nanobacteria with periodontal disease and its cardiovascular implications.

Association between nanobacteria and periodontal disease.

We found that incident tooth loss was significantly associated with PAD, especially among men with periodontal diseases. The results support a potential oral infection-inflammation pathway.

Comment: There is an obvious need to monitor and deal with periodontal disease because of its established link to cardiovascular disease, inflammation and elevated CRP.


Sugar Intake Related to Cardiac CRP Increase
Dietary glycemic load is significantly and positively associated with plasma hs-CRP in healthy middle-aged women, independent of conventional risk factors for ischemic heart disease. Exacerbation of the proinflammatory process may be a mechanism whereby a high intake of rapidly digested and absorbed carbohydrates increases the risk of ischemic heart disease, especially in overweight women prone to insulin resistance.

Comment: once again the “benefits” of sugar are in evidence. See our website www.professionalco-op.com Research page for lots more on sugar in the Syndrome X paper.


Statins Lower CRP
Recent evidence shows that statin drugs not only lower LDL-cholesterol levels but are also have potent anti-inflammatory effects as well.

Comment: It should be noted that statins also deplete co enzyme Q-10.

Statins as potent anti-inflammatory drugs. Lefer DJ. Circulation 2002;2041-2

Anti-inflammatory Agents Lower CRP and May Benefit Cardio Vascular Disease
The base-line plasma concentration of C-reactive protein predicts the risk of future myocardial infarction and stroke. Moreover, the reduction associated with the use of aspirin in the risk of a first myocardial infarction appears to be directly
related to the level of C-reactive protein, raising the possibility that anti-inflammatory agents may have clinical benefits in preventing cardiovascular disease.

*New England Journal of Medicine* 1997; 336:973-979

**Anti-Inflammatory Nutrients**

Many studies have shown that dietary supplements can assist the body's ability to control and reduce inflammation. There is a considerable list of possible anti-inflammatory nutrients including quercetin, enzymes such as serrapeptase, nattokinase, bromelain/papain and pancreatic enzymes; herbs including: ginger, cayenne, boswellia, turmeric (curcumin) and green tea. Below are some studies that relate selected nutrients to CRP.

In general, we believe it wise to limit high doses of any nutrient to therapeutic short-term use as needed. Whole organic foods, when possible, are highly desirable as is pure water of proper pH, redox and mineralization.

**Fish oil**

Fish oil supplements, rich in EPA and DHA, bypass the body's need to convert alpha linolenic acid (ALA) to EPA and DHA.

Eicosapentaenoic acid (EPA) (171 mg/capsule) and docosahexaenoic acid (DHA) (114 mg/capsule). Patients received either 10 Maxepa or air-filled placebo capsules per day for 12 months. These patients were able to reduce their NSAID requirement without experiencing any deterioration in the clinical and laboratory parameters of RA activity. *Lau CS, Morley KD, Belch JF. Effects of fish oil supplementation on non-steroidal anti inflammatory drug requirement in patients with mild rheumatoid arthritis - a double-blind placebo controlled study. British Journal of Rheumatology, 1993;32:982-989.*

The potential pathogenicity of free radicals may have a pivotal role in ulcerative colitis. Fish oil omega-3 fatty acids exert anti-inflammatory effects on patients with ulcerative colitis (UC). Disease activity was assessed by laboratory indicators (C-reactive protein, alpha(1)-acid glycoprotein, alpha(1)-antitrypsin, erythrocyte sedimentation rate, albumin, hemoglobin, and platelet count) The results suggested that omega-3 fatty acids may act as free radical scavengers protecting the patients against the overall effect of oxidative stress.


**GLA (Gamma Linolenic Acid)**

Administration of gamma linolenic acid (GLA), an unsaturated fatty acid, reduces joint inflammation in patients with rheumatoid arthritis. GLA boosts levels of prostaglandin E1, which reduces inflammation caused by prostaglandin E2. GLA supplements are derived from evening primrose, borage, or black currant oils. *Gamma linolenic Acid, an Unsaturated Fatty Acid with Anti-Inflammatory Properties, Blocks Amplification of IL-1β Production by Human Monocytes Robert K. Furse, Ronald G. Rossetti and Robert B. Zurier Department of Medicine, Division of Rheumatology, University of Massachusetts Medical School, Worcester, MA 01655. The Journal of Immunology, 2001, 167: 490-496.*

**CLA (Conjugated Linoleic Acid)**


**ALA (Alpha-Linolenic Acid from linseed (flax) and rapeseed oils)**

Inflammation plays an important role in the pathogenesis of coronary artery disease. C-reactive protein (CRP), serum amyloid A (SAA), and interleukin-6 (IL-6) levels were determined prior and after intervention. Dietary supplementation with ALA for 3 months decreases significantly CRP, SAA and IL-6 levels in dyslipidaemic patients. This anti-inflammatory
effect may provide a possible additional mechanism for the beneficial effect of plant n-3 polyunsaturated fatty acids in primary and secondary prevention of coronary artery disease **Comment:** Flax oil also inhibits platelet adhesiveness.


**Beta Carotene**

Compared with controls, patients had signs of an enhanced inflammatory activity assessed by significantly increased levels of CRP, sIL-2R and CD4+CD25+T cell subsets. Patients also had significantly lower beta-carotene and lycopene levels whereas α-tocopherol levels did not differ. Low serum beta-carotene in CAD patients reflects activation of the immune system. Inflammation should be considered as an important confounding factor when analyzing data on beta-carotene and CAD.


**Vitamin E**

Several clinical studies have found that natural vitamin E can significantly lower CRP and IL-6 levels. This effect may account for the vitamin's well-known heart benefits. The anti-inflammatory benefits of vitamin E were also noted in two clinical trials that found the vitamin of benefit in patients with rheumatoid arthritis.

Alpha Tocopherol (Vitamin E) supplementation significantly lowered levels of C-reactive protein and monocyte interleukin-6 in all test groups. AT therapy decreases inflammation in diabetic patients and controls and could be an adjunctive therapy in the prevention of atherosclerosis. Dose was 1200 IU/day. CRP levels dropped by 30%.

**Comment:** While no reference I given for CRP, it is noteworthy that Dr. Hans Nieper used this substance in cardiovascular patients. **DOSE:** 30-40 mg./day in divided dose on an empty stomach.


**Vitamin C**

Peripheral arterial disease (PAD) is a severe atherosclerotic condition frequently accompanied by inflammation and oxidative stress. In stepwise multivariate analysis, low L-ascorbic acid concentration in PAD patients was associated with high CRP level.

*Serum vitamin C concentration is low in peripheral arterial disease and is associated with inflammation and severity of atherosclerosis.* Langlois M, Duprez D, Delanghe J, De Buyzere M, Clement DL. *Circulation.* 2001 Apr 10;103(14):1863-8.

**Serrapeptase Enzyme**

The effect of serrapeptase (Aniflazym) on post-operative swelling and pain was carried out in 3 randomized groups of patients. In the group receiving the test substance, the swelling had decreased by 50% on the third post-operative day, while in the other two control groups no reduction in swelling had occurred at that time. Decreasing pain correlated for the most part with the reduction in swelling.

**Comment:** While no reference I given for CRP, it is noteworthy that Dr. Hans Nieper used this substance in cardiovascular patients. **DOSE:** 30-40 mg./day in divided dose on an empty stomach.


interleukin-6 levels in normal volunteers and type diabetic patients.

Devaraj S, Jialal I. Departments of Pathology University of Texas Southwestern Medical Center, Dallas, TX 75390-9073, USA.
Next Month’s Topic: Homocysteine

Your comments and suggestions are welcome and may be included in future newsletters.

Thank you!

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FDA has not commented on the above-mentioned studies or statements

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