

LE Magazine December 2002

REPORT

C-Reactive Protein

A better diagnostic tool than cholesterol
for predicting cardiovascular disease risk

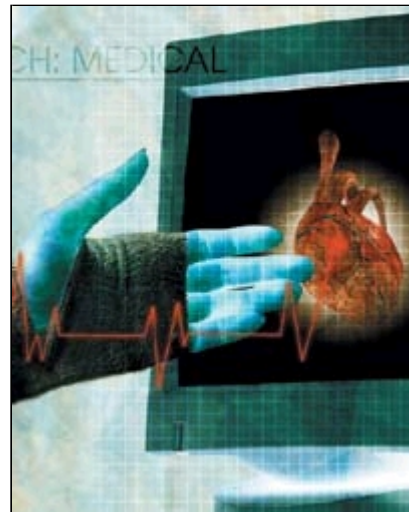
Mainstream medicine has adopted cholesterol-lowering therapies as its first-line defense against heart attack. Millions of people swallow drugs each day to keep their cholesterol low, and drug companies continue to campaign aggressively to get more people to take these medications. A review of the scientific evidence, however, shows that measurements of an inflammatory marker in the blood called C-reactive protein can yield better diagnostic information than measurements of cholesterol. The C-reactive protein test is inexpensive and simple, but most physicians don't yet perform it. When doctors for George W. Bush measured his C-reactive protein levels, they had to consult with a research team to find out how to analyze his results![1]

A chronic inflammatory state, as evidenced by elevated C-reactive protein, results in significant damage to the arterial system.

A series of landmark studies by Paul Ridker, M.D. and colleagues indicates that 25 to 35 million Americans have total cholesterol within normal range but above-average levels of inflammation within their cardiovascular systems, and that this inflammation has significant impact on heart disease risk.[2-5] The Women's Health Study, which involved 39,876 healthy postmenopausal women, supports the C-reactive protein link to cardiovascular disease.[6] Those with the highest levels of C-reactive protein had five times the risk of developing cardiovascular disease and seven times the risk of having a heart attack or stroke compared to subjects with the lowest levels. C-reactive protein levels predicted risk of these events even in women who appeared to have no other pertinent risk factors.

The Physicians' Health Study, which evaluated C-reactive protein levels and heart disease risk in 22,000 initially healthy men, also supports the relationship between inflammation and heart attack.[7] Inflammation may explain why women taking Premarin have slightly increased risk of heart attack; Premarin causes C-reactive protein levels to climb.[8] Data from the Framingham cohort correlated high C-reactive protein with calcification of the coronary arteries.[9]

Research on C-reactive protein indicates that cholesterol-filled plaques in blood vessels may not pose any real danger unless they are affected by inflammation. Inflammation weakens plaques, making them more vulnerable to bursting or pinching off a clot that can then block coronary vessels.[10-13]



AN INFLAMMATION PRIMER

Inflammation is an immune response that occurs after infection or injury. It involves a series of biological actions that leads to the development of redness, heat and swelling. All of these elements are created by the activity of immune cells working to break down injured and dying tissues so that new, healthy ones can replace them. When you suffer a painful bump after hitting your head, that's inflammation at work. When you develop a fever in response to an infection, you're experiencing a form of full-body inflammation that creates an inhospitable environment for multiplying pathogens. A boil is a highly localized inflammation, while a sunburn is an inflammation that can cover large areas of skin.

In any case, inflammation involves a delicate balance: if the body's inflammatory response is too intense, harm can come to otherwise healthy tissues. The production of C-reactive protein is an essential part of the inflammatory process, and the measurement of this substance reflects the level of inflammatory activity deep within the body. It appears that certain conditions create a state of excessive inflammation within the circulatory system. High C-reactive protein levels are evidence of this type of inflammation.

Inflammation accelerates the production of free radicals. When inflammation is limited, free radicals can be controlled by antioxidant defenses; in fact, the free radicals help the body get rid of pathogens and make way for healing. But when inflammation is chronic or intense, free radicals can do more harm than good. They can do significant damage to tissues and set in motion harmful chain reactions.

Allergies, asthma, eczema, autoimmune disease and some types of arthritis are chronic forms of low-grade inflammation. The immune system mounts defenses that go beyond what is necessary, reaching an elevated plateau where inflammation becomes damaging to otherwise healthy tissues.



What is the source of this inflammation? Researchers have a few different theories. Some posit that plaques are actually an attempt on the part of the immune system to repair some sort of damage to vessel walls. According to this theory, the inflammation arises as the body sends immune factors to the damaged area. Other theories implicate pathogens, including *Chlamydia pneumoniae* and the ulcer-causing *Helicobacter pylori*. Some research has indicated that people who are seropositive for these pathogens are at significantly elevated risk of a cardiac event,[14,15] and that this may be due to a state of chronic, low-level inflammation spurred by the continued presence of the bacteria.

Well-established cardiac risk factors such as obesity, smoking, hypertension and chronic periodontal disease all increase inflammation and C-reactive protein levels in the body. Fat cells literally pump out C-reactive protein, which could explain why being overweight is so bad for the heart.[16]

The real diet-heart connection

The so-called low-fat, low-cholesterol “heart-healthy diet” may actually end up promoting inflammation. Although a diet of whole foods that includes plenty of vegetables and fruits will not have this effect, the average American’s low-fat diet rarely fits this description. Diets low in foods that supply omega-3 fatty acids and high in refined grains and other processed foods usually supply fat in the form of polyunsaturated vegetable oils and hydrogenated oils. This dietary profile creates an imbalance of essential fats in the body, with the intake of omega-6 oils and hydrogenated oils far exceeding the intake of omega-3 fats.

Alzheimer’s, Diabetes and C-Reactive Protein

Inflammatory processes have also been implicated in Alzheimer’s disease. Subjects enrolled in the Honolulu-Asia Aging Study were three times more likely to develop Alzheimer’s during a 25-year follow-up if they were in the highest quartile of C-reactive protein levels (compared with those in the bottom quartile). A correlation was evident: the more C-reactive protein subjects had at the start, the higher their risk of developing Alzheimer’s disease.*

Diabetics have elevated markers of deep inflammation. Research by Dr. Ridker and colleagues have provided support for a common inflammatory basis of these two diseases — illnesses that often strike in the same individuals.**

Omega-3 and omega-6 fats are the raw materials from which eicosanoids, hormonelike substances with multiple effects on body systems, are made. One of the most important duties of eicosanoids is to regulate inflammation, and their manufacture depends upon the supply of fats in the diet. When the appropriate balance of omega-6 to omega-3 is consumed,[17] inflammation is kept in check, occurring when necessary to heal the body but rarely getting out of hand. With a diet high in omega-6 vegetable fats and low in omega-3 fats, eicosanoid production shifts accordingly. The end result is greater inflammation. An excess of saturated fats from meats and dairy products also encourages pro-inflammatory eicosanoid production.

C-reactive protein control

If you are forty years old or older, insist that your doctor prescribe a C-reactive protein test for you the next time you have your cholesterol measured.

Some members of the research community have suggested that statin drugs—the drugs of choice for cholesterol reduction—may prevent heart disease not because of their effects on cholesterol, but because they have anti-inflammatory activity. This helps to explain why statins have been found to protect the heart regardless of their effects on cholesterol levels.[18,19]

Aspirin, too, has consistently been found to lower the risk of heart attack. The inflammation-heart disease connection could explain this effect, rather than the blood-thinning (anti-platelet) effect to which this decrease in risk has been attributed. Some evidence indicates that ibuprofen may also provide protection against elevated C-reactive

protein and the damage it can do.[20]

Vitamin E's ability to protect against heart disease has also been attributed to its blood-thinning effects, but recent research has shown that it lowers C-reactive protein levels considerably.[21,22]

Low levels of the steroid hormone DHEA have been correlated with increased C-reactive protein levels in rheumatoid arthritis (RA) patients. A ketogenic (low-glycemic) diet and fasting both lowered C-reactive protein levels, raised DHEA levels, and improved symptom states in people with RA.[23] Although more research is needed on this topic, the prudent use of DHEA replacement seems to be a promising avenue in heart disease prevention.

An anti-inflammatory diet includes abundant fresh vegetables and fruits, small servings of whole grains and protein from fish (especially salmon, mackerel, cod, sardines and other deep-sea-dwelling species). Pumpkin seeds, walnuts and flaxseeds are excellent sources of omega-3 fats. Ground flaxseeds can be added to whole grains or sprinkled onto salads to augment omega-3 intake. Avoid corn, soy and cottonseed oils, especially those that have been hydrogenated. Instead, use olive or canola oil when added fats are called for. You can also use butter, but do so moderately.

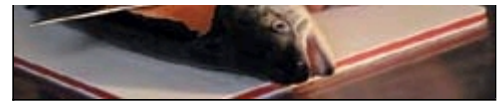


* Schmidt R, Early inflammation and dementia: a 25-year follow-up of the Honolulu-Asia Aging Study, Ann Neurol 2002 Aug;52(2):168-74.

** Pradhan AD, Ridker PM, Do atherosclerosis and type 2 diabetes share a common inflammatory basis? Eur Heart J 2002 Jun;23(11):831-4.

One of the best ways to control inflammation is to take fish oil supplements daily. Fish oil supplements should contain both DHA (docosahexaenoic acid) and EPA (eicosapentaenoic acid). A recent study[24] found that three grams of fish oil a day was heart-protective. Antioxidant supplements help to control free radicals produced by inflammation.





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