EDUCATIONAL COMMENTARY – C-Reactive Protein

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Learning Outcomes
Upon completion of this exercise, participants will be able to:

- define acute-phase reactant/acute-phase protein.
- discuss the uses of C-reactive protein.
- compare C-reactive protein with the erythrocyte sedimentation rate.
- discuss the relationship of the C-reactive protein concentration and the risk of a future cardiovascular event.

Infections, autoimmune diseases, chronic inflammatory bowel syndrome, trauma, or cancer can cause inflammation. When inflammation occurs, the body responds by producing significantly increased concentrations of certain substances. When inflammation subsides, inflammatory protein concentrations will decrease. Because the protein concentration parallels a person’s inflammatory status, these substances are classified as acute-phase reactants. They are also known as acute-phase proteins. Acute-phase proteins are primarily produced in the liver. C-reactive protein (CRP) is one of these acute-phase proteins. It is normally found in very low concentrations in the blood, less than 5 mg/L (0.5 mg/dL). However, when acute inflammation is present, CRP concentration can increase very quickly and is used as a nonspecific marker of inflammation. An elevated level of CRP indicates that inflammation is present, but it does not suggest the source of the inflammation. Other testing must be performed to determine the cause of the inflammation. In acute inflammation, the concentration of CRP may increase to a level as much as 40,000 times the normal value. CRP begins to rise within six hours of the onset of the inflammatory process, and peaks at about 48 hours after the onset. When the inflammation subsides, CRP levels quickly return to normal.

Acute-phase proteins play an important role in the immune response. Some acute-phase proteins act in conjunction with other immune mechanisms to inhibit or destroy microorganisms. Other acute-phase proteins enhance coagulation to wall off or limit the growth of pathogens by surrounding them with a blood clot. Complement components, haptoglobin, and alpha-1-antitrypsin are other examples of acute-phase proteins. Low concentrations of acute-phase proteins are associated with liver failure.

CRP measurements quickly detect infection in patients who have recently undergone surgery. If an increased level of CRP persists for three days after surgery, the patient may have an infection. Early detection is an important component of successful therapy. By monitoring CRP levels, physicians can also determine the effectiveness of treatments or determine the progress of inflammatory diseases such
as rheumatoid arthritis or systemic lupus erythematosus. In these diseases, an elevated CRP level can indicate an acute flare-up, while a decrease in CRP concentration can be evidence of remission.

Erythrocyte sedimentation rate (ESR or sed rate) is also often performed to detect inflammation. While the ESR also rises when inflammation occurs and falls when inflammation subsides, it does not respond as quickly to changes in inflammation. Therefore, the CRP level can be negative, while the ESR remains elevated in a patient whose inflammation has subsided. Also, because the CRP level rises more quickly after the onset of inflammation, the ESR can be negative when the CRP level is elevated in a patient with a new infection or inflammatory state. Therefore, CRP is a more useful marker of inflammation than the ESR.

The risk of cardiovascular disease (CVD) has long been associated with age, family history of heart attack or stroke, gender, high blood pressure, obesity, smoking, and the lack of physical activity. Total cholesterol, HDL (high-density lipoprotein) cholesterol, and LDL (low-density lipoprotein) cholesterol levels are monitored risk factors for CVD. However, some individuals do not have abnormal levels and still experience cardiovascular events. In the 1990s, research provided an expanded list of tests to uncover risk factors for predicting CVD. These tests include homocysteine, lipoprotein A, fibrinogen, and CRP. Inflammation was shown to play an important role in atherosclerosis. A more sensitive test for CRP—high-sensitivity CRP (hs-CRP)—was developed to accurately measure CRP at very low levels. The Harvard Women's Health Study studied the relationship between a cardiovascular event (heart attack or stroke) and hs-CRP, LDL cholesterol, and HDL cholesterol. High-sensitivity-CRP was found to be a better predictor of a future cardiac event than LDL cholesterol or HDL cholesterol.1

In a patient with cardiovascular disease, CRP works in conjunction with complement to enhance the immune response when a coronary artery containing plaque is injured. The immune response produces an inflammatory state. Plaque is a buildup of lipids in the artery. When the plaque is disrupted, a clot forms and the flow of blood to the heart can be blocked. One of the results of inflammation is swelling, thus further reducing the diameter of the artery. A heart attack occurs when there is ischemia, or a lack of blood flow to the heart muscle, followed by death (necrosis) of the heart muscle. The level of CRP in a healthy person without inflammation associated with an infection is less than 5 mg/L (0.5 mg/dL). Levels greater than 3 mg/L (0.3 mg/dL), indicate low-level inflammation and an increased risk of cardiovascular disease. When CRP levels are greater than 10 mg/L (1.0 mg/dL), the source of the inflammation is most likely an infection rather than inflammation of the arteries. High-sensitivity CRP is not used alone in assessing the risk of cardiovascular disease, but it is helpful when considered along with the patient's symptoms, the patient's risk factors, and other related tests including total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides.
According to the American Heart Association, the relationship between hs-CRP concentration and the risk of cardiovascular event risk is:

- Low risk: Less than 1.0 mg/L (< 0.1 mg/dL)
- Average risk: 1.0 - 3.0 mg/L (0.1 - 0.3 mg/dL)
- High risk: Greater than 3.0 mg/L (>0.3 mg/dL)

In conclusion, the traditional assay for CRP detects the presence of inflammation in surgical patients and monitors the response to therapy in patients with infections or chronic inflammatory autoimmune diseases. The newer more sensitive assays for CRP help clinicians predict future cardiovascular and stroke events. The American Heart Association does not currently recommend screening the general public for hs-CRP. However, those at known risk of heart disease, high blood pressure, diabetes, high cholesterol, and a family history of heart disease should be screened.

Reference