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# The Inflammatory Heart Diseases: Causes, Symptoms, and Treatments

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**Abstract** The inflammation of the heart muscles, such as myocarditis, the membrane sac which surrounds the heart called as pericarditis, and the inner lining of the heart or the myocardium, heart muscle as endocarditis are known as the inflammatory heart diseases. Inflammation of heart is caused by known infectious agents, viruses, bacteria, fungi or parasites, and by toxic materials from the environment, water, food, air, toxic gases, smoke, and pollution, or by an unknown origin. Myocarditis is induced by infection of heart muscle by virus like sarcoidosis and immune diseases. The symptoms include chest pain, angina, pain in heart muscle, and shortness of breath, edema, swelling of feet or ankles, and fatigue. The ECG, X-ray, and MRI can diagnose the disease; blood test and rise in enzymes levels provide abnormality in heart function. The treatment includes use of antibiotics for inflammation of heart muscle and medications. The ultrasound imaging indicates further damage to the heart muscle. In severe cases of infection heart failure can occur so long-term medications are necessary to control inflammation. The various biomarkers are reported for the inflammatory heart diseases. The causes, symptoms and treatments of inflammatory heart diseases are described.

**Keywords** Inflammatory heart diseases · Infectious agents · Imaging

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## Introduction

There are three main types of known inflammatory heart diseases, the myocarditis, pericarditis, and endocarditis [1]. These are as follows:

Myocarditis

It is the infection which occurs within the heart muscle induced by viruses like sarcoidosis, and distinct immune diseases. The virus attacks the heart muscle and results in local inflammation. Myocarditis continues to plague the heart muscle long after the infection has ceased. There are some symptoms of this disease which is asymptomatic. Myocarditis as well as angina produces pain in the chest and heart muscles. It may progress into degeneration of the heart muscle. This may trigger to heart failure if it is not treated well before. Usually, symptoms of shortness of breath, difficulty in breathing, edema of heart, or swelling of feet and ankles, fatigue, tiredness, exhaustion, and other symptoms. Myocarditis is diagnosed by ECG, electrocardiogram which detects deviations within the heartbeat. The MRI, magnetic resonance imaging provides the pictures of heart muscle peculiarities or abnormalities, swelling or water in the heart. Blood test is performed which indicates the biochemical and enzymological profile of the blood, where rise in enzymes levels of heart muscle are found in myocarditis. The prognosis is an uncertainty about recovery in the early phase of myocarditis. In severe cases due to infection and damage to the heart muscle, the heart failure can occur. If the infection is very serious, the heart

transplant by surgery is required. If the degeneration of heart muscle is enormous, a defibrillator is implanted so that heart can function better.

Pericarditis

It is a heart disease that causes inflammation of the pericardium. The pericardium is the fluid sac that envelopes the heart and provides lubrication to the heart and decreases the friction during activity and firmly secures the heart to the surrounding walls within the thoracic cavity. The causes of pericarditis include some tumors or cancer; the metabolic disorders of hypothyroidism and uremia, kidney failure; infection by viruses or bacteria; heart attack, trauma, and heart surgery; a connective tissue disease as sarcoidosis and rheumatic arthritis; and an unexpected reaction to certain types of medications. Pericarditis symptoms include chest pain, or angina pectoris, pain which travels from chest to shoulder blades, back and neck. The pain near the diaphragm that extends to the back, when inhaling deeply the chest pain becomes worse and unbearable when lying, and becomes better when leaning forward. The pain may occur in the esophagus when swallowing food or water due to inflammation, and some fever may develop due to infection. Pericarditis is diagnosed by pain in chest, a pericardial friction rub may be detected by a stethoscope, which is due to inflammation of heart, the ECG, chest X-ray confirms the disease, and ultrasound imaging provide information for pericarditis. A blood test and rise in enzymes levels can confirms the disease. The treatment for Pericarditis is the administration of anti-inflammatory medications which reduce inflammation of heart muscle. Ibuprofen is the medicine used frequently for pain and anti-inflammatory properties. Morphine or some narcotic pain medications can be used. Pericardiocentesis removes the excessive fluid from the sac and detects the pathogenic organisms which induce inflammation and pericarditis.

Endocarditis

It is induced by an infection of the endocardium or inner lining of the heart resulting in pronounced inflammation. When pathogens from other regions of the body infect the blood-stream and fix themselves to defective areas of the heart the disease can occur. If it is not treated early it may cause partial or complete damage to the heart valve or may cause a heart failure. It usually affects people who have an artificial heart valve in place or have suffered degeneration of a heart valve. The preexisting heart defects also increase the development of this disease. But it does not affect normally healthy people. Endocarditis symptoms may develop over a long period of time or manifest suddenly, and its progression depends on the heart defect or infection. The Endocarditis symptoms include sudden weight loss; joint and muscular pain; fever and chills; visible purple or red spots exhibited in the mouth, skin or on whites of the eyes; heart murmurs (irregular sounds arising from the heart); constant coughing; blood in the urine; oedema, and swelling of the feet and abdomen; fatigue and unusual tiredness; night sweats; tenderness below the rib cage which is associated with the spleen; a pale face or complexion; areas of red tender spots just below the skin of the fingers; and shortness of breath or difficulty in breathing. Although these symptoms may look similar to other non-threatening conditions it is necessary to see a physician when these symptoms are observed if affected by another heart defect. People who are at risk are individuals who currently have an artificial valve(s) by heart surgery. The artificial valves are more susceptible to the infection by bacteria and viruses which are most notably in the first year of implantation. So antibiotics are necessary to take after surgery. In case of a congenital heart defect at birth which means the heart is more likely to be affected by the infections. The previous injury to the heart can also increase the susceptibility. The intravenous drug users are at a great risk of developing the condition because of needle sharing and infection. The bacteria in this condition are found commonly in contaminated needles. The endocarditis diagnosis includes blood test, and ECG which provides information of bacterial infection. The Echocardiogram is taken to properly see if the heart condition has inflammation or infection. The ECG or electrocardiogram and X-ray are also used to confirm the diagnosis of disease. The MRI, magnetic resonance imaging, and CT, computerized tomography scan are used if it is believed the infection may have traveled to other parts of the body. The treatments are mainly antibiotics, and medications, or may be surgery if the damage to the heart is serious due to infection.

## Markers of Inflammatory Heart Diseases

The markers of inflammation and cardiovascular disease have been reported in AHA/CDC scientific statement [2]. Several biochemical or enzymatic markers have been suggested for the determination of inflammatory diseases of heart. However, their routine uses for the risk assessment of inflammatory heart diseases are not yet considered applicable because of lack of measurement standardization; lack of consistency in epidemiological findings from prospective studies with endpoints; and lack of evidence that the novel marker adds a risk prediction over and above what is already achievable through the use of established risk factors [3, 4]. Several commercial bioassays for inflammatory markers for heart diseases are available, but how to use such bioassays of markers of inflammation of

bacteria and viruses daily for the clinical practice is not clear yet [2]. A Workshop of AHA/CDC, March 14, 15, 2002 in Atlanta, Georgia, US, on the Inflammatory Markers and Cardiovascular Disease, took place for clinical application of markers for such heart diseases. The most useful tests for heart diseases and bioassays were determined. To achieve this goal, the workshop set down five objectives:

(1) To review the scientific evidence from diverse sources to examine the association between several inflammatory markers (high-sensitivity C-reactive protein (hs-CRP), serum amyloid A (SAA), and white blood cell (WBC count, fibrinogen, etc.) and cardiovascular diseases including the strength, consistency, independence, and generalizability of the data.
(2) To consider the clinical chemistry and various assays of inflammatory markers, to identify which may be the best bioassay to use in identifying patients at risk.
(3) To identify areas in which questions persist in order to foster additional research on inflammatory markers and CVD.
(4) To recommend which tests should be performed for patients and in which clinical settings, for the purpose of risk stratification, therapeutic monitoring, and other clinical applications, on the basis of the scientific evidence.
(5) To explore the public health implications of an association between inflammatory markers and CVD.

This conference was jointly sponsored by the Centers for Disease Control and Prevention (CDC) and AHA. The National Center for Chronic Disease Prevention and Health Promotion and the National Center for Environmental Health provided financial and organizational support. The AHA, its expert panel on population and prevention science, and its councils on atherosclerosis, thrombosis, and vascular biology; clinical cardiology; and epidemiology and prevention coordinated the workshop, with support from unrestricted educational grants from industry sponsors. The writing group, endorsed by the Science Advisory and Coordinating Committee of the AHA, included representation from the above-mentioned agencies and organizations, as well as the Amer. Association for Clinical Chemistry and the Amer. College of Cardiology [4].

## Inflammation as a Key Pathogenetic Mechanism in Atherosclerosis

A role for inflammation is well established describing the atherosclerotic disease process [5, 6]. All the stages, initiation, growth, and complication of the atherosclerotic plaque [7, 8] is considered to be an inflammatory response to injury. The major injurious factors that promote atherogenesis, cigarette smoking, hypertension, atherogenic lipoproteins, and hyperglycemia are well established. These risk factors give rise to a variety of noxious stimuli that elicit secretion of both leukocyte soluble adhesion molecules, which facilitate the attachment of monocytes to endothelial cells, and chemotactic factors, which encourage the monocytes' migration into the subintimal space. The transformation of monocytes into macrophages and the uptake of cholesterol lipoproteins are thought to initiate the fatty streak. Further injurious stimuli may continue the attraction and accumulation of macrophages, mast cells, and activated T cells within the growing atherosclerotic lesion. Oxidized low-density lipoproteins, LDL, may be one of several factors that contribute to loss of smooth muscle cells through apoptosis in the atherosclerotic plaque cap, and secretion of metalloproteinases and other connective tissue enzymes by activated macrophages may break down collagen, weakening the cap and making it prone to rupture. This disruption of the atherosclerotic plaque then exposes the atheronecrotic core to arterial blood, which induces thrombosis. Thus, virtually every step in atherogenesis is believed to involve cytokines, other bioactive molecules, and cells that are characteristic of inflammation. These pathophysiological insights provide potential targets for measurement as a means to identify and monitor the ongoing inflammatory process. Potential targets for measurement include proinflammatory risk factors such as oxidized LDL, proinflammatory cytokines (e.g., Interleukin-1, Tumor necrosis factor-α), adhesion molecules (intercellular adhesion molecule-1, selectins), inflammatory stimuli with hepatic effects (e.g., interleukin-6) or the products of the hepatic stimulation, such as SAA, C-reactive protein (CRP), and a host of other acute-phase reactants. Finally, other indicators of cellular responses to inflammation, such as elevated leukocyte count, might be evaluated. This inflammatory case may have sources other than an atherosclerotic coronary artery, including atherosclerosis in other arteries, as well as systemic inflammation (e.g., connective tissue diseases) and local infections (gingivitis, prostatitis, bronchitis, urinary tract infections, and gastric inflammation). These inflammations may result in elevated levels of inflammatory markers that may be attributed to atherosclerotic CVD. The increasing recognition of the inflammatory component of atherogenesis provides the biological doubt for the potential use of inflammatory markers as indicators of atherogenesis or as predictors of atherosclerotic complications. More research is needed for the biomarkers of atherosclerosis disease and inflammation where cholesterol, LDL and plaques are formed in the coronary arteries of the heart.

## Characteristics for CVD Risk Predictors

The consideration of a number of inflammatory markers is useful as predictors of prevalent or incident of CVD (Figure, [2]. Such markers may or may not be useful in the clinical study unless they possess some characteristics [9]. These include ability to standardize the bioassay, determine the risk factors for CVD, and endpoint for clinical trials. Generally, the biomarkers results are acceptable to understand the inflammatory processes of heart. Many biochemical or enzymological methods are used for bioassays of markers for heart diseases. The use of inflammatory markers is a challenging field for future advancement for short-term or long-term studies of heart diseases. Some biomarkers studies have shown promising results for the detection of many heart diseases or other diseases [10–16]. In Fig. 1, the inflammatory factor model is shown for the risk of heart disease [2].

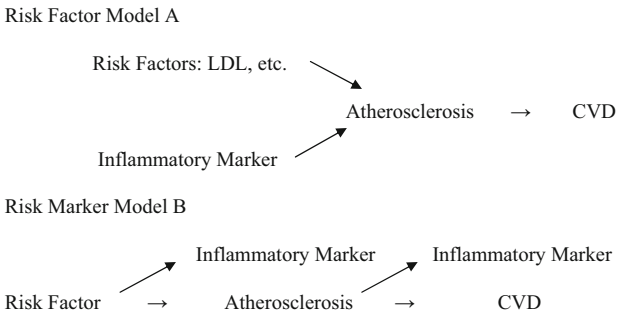


**Fig. 1** Inflammatory markers model for risk of heart disease

## Biomarkers of Myocarditis

The Tenascin-C (TNC) is a useful biomarker for the detection of myocarditis disease [17]. Tenascin-C (TNC) is an extracellular matrix protein which appears at active sites of tissue remodeling during embryogenesis or cancer invasion. In normal heart, TNC is only present during the early stages of development but reappears in pathological states [17]. Expression of TNC was examined in myosin-induced autoimmune myocarditis mice models. Sequential changes in amount, localization and the producing cells were analyzed by reverse transcriptase-polymerase chain reaction, Western blotting, immunohistochemistry and in situ hybridization, and compared with the histological picture. The expression of TNC was up-regulated at a very early stage of myocarditis. Immunostaining was detectable before cell infiltration and myocytolysis became histologically apparent, remained during the active stage while cell infiltration and necrosis continued, and disappeared in scar tissue with healing. TNC immunostaining was always observed at the periphery of necrotic or degenerating cardiomyocytes in foci of inflammation, the expression level correlating with histological evidence of inflammatory activity. Interstitial fibroblasts were the major source of TNC, expressing the large isoform containing alternative splicing sites. These data demonstrate that TNC is a useful marker for evaluation of disease activity in myocarditis [17].

## Biomarkers of Pericarditis

Cardiac biomarkers are frequently considered part of the diagnostic tool kit but are sometimes elevated in patients with acute pericarditis because of the inflammatory process involving the epicardium with subsequent myocardial necrosis [18]. The incidence of increased cardiac Troponin I levels in patients with viral or idiopathic acute pericarditis has been reported as 32.2 %; of these patients, 23.7 % had a Troponin I level at admission that was beyond the AMI threshold. The temporal relationship of troponin elevation may be remarkably similar to that seen in AMI. The prognostic implication of elevated Troponin level is largely benign in acute pericarditis. The increased level of troponin in blood of patients in pericarditis disease can be a useful biomarker for the detection of pericarditis disease.

## Biomarkers of Endocarditis

The infectious endocarditis is a bacterial infection of the endocardium. The diagnosis is based on the results obtained from echocardiography, blood cultures, and molecular genetic screening for bacteria and on data for inflammatory markers such as the leukocyte (WBC) count, and the C-reactive protein (CRP) concentration. The aim of study was to evaluate lipopolysaccharide-binding protein (LBP) as a supportive biomarker for the diagnosis and therapeutic monitoring of IE [19]. The LBP and CRP concentrations and WBC counts were measured in 57 IE patients at hospital admission, 40 patients with noninfectious heart valve diseases (HVDs), and 55 healthy blood donors. The progression of these 3 markers and the influence of cardiac surgery on them were evaluated in 29 IE patients and 21 control patients. The results indicated serum LBP concentrations were significantly higher in IE patients (mean (SD), 33.41 (32.10) mg/L) compared with HVD patients (6.67 (1.82) mg/L, $P < 0.0001$) and healthy control individuals (5.61 (1.20) mg/L). The progression in the LBP concentration during therapy of IE patients correlated with the changes in the CRP concentration. The 2 markers were equally influenced by antibiotic treatment and surgical intervention. The conclusion was that the serial LBP measurement may provide an effective and useful

tool for evaluating the response to therapy in IE patients. A strong correlation was found between LBP and CRP concentrations; LBP has a tendency to increase earlier in cases of reinfection. The lipopolysaccharide-binding protein (LBP) is a supportive biomarker for the diagnosis and therapeutic monitoring of endocarditis.

## Conclusion

The three types of Inflammatory heart diseases are known as inflammation of the heart muscle, myocarditis, the membrane sac which surround the heart called as pericarditis, and inner lining of heart myocardium, as endocarditis. Inflammation of heart is caused by infectious agents, such as viruses, bacteria, fungi, parasites, and by toxic materials from environment, water, food, toxic gases, smoke, air pollution, or by an unknown origin. Myocarditis is induced by infection of heart muscle by virus like sarcoidosis and immune diseases. The symptoms include chest pain, angina, pain in heart muscle, and shortness of breath, edema, swelling of feet or ankles, and fatigue. The ECG, X-ray, and MRI can diagnose the disease. The blood test and rise in enzymes levels provides abnormality in heart function. Treatment includes use of antibiotics and medications. The ultrasound imaging also indicates damage to heart muscle. In case of severe infection the heart failure may occur. Therefore, long-term medications are necessary to control inflammation. The various biomarkers have been reported for the detection of inflammatory heart diseases. The causes, symptoms, and treatments of inflammatory heart diseases are mentioned.

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