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New Blood Tests for Detecting Heart Disease

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Heart disease is the primary cause of illness and death in the United States.

- 50 000 000 patients have hypertension
- 7 600 000 patients suffer a myocardial infarction each year
- 4 900 000 patients have been diagnosed with congestive heart failure[1]

Because improved detection of heart disease can save lives, blood tests have been used for approximately 50 years to detect substances that are present in the blood that indicate either disease or a future risk of the development of a disease (Table). Blood tests detect substances that normally are not present or measure substances that, when elevated above normal levels, indicate disease.

Tests to Detect Heart Attacks

Patients presenting to the emergency department with chest discomfort will have an initial assessment for a possible heart attack (myocardial infarction). Electrocardiograms (ECGs or EKGs) are used in the evaluation of patients with chest discomfort but can be normal or not diagnostic in patients with a myocardial infarction. Thus, blood will be obtained to check for any heart damage that can be indicated by abnormal protein levels in the blood. The specific proteins that are the subjects of these blood tests include:

- Creatine kinase (CK)
- Creatine kinase-MB (CKMB)
- Myoglobin
- Cardiac troponin I or cardiac troponin T

These proteins are normally present within the heart cells and are released into the blood after a heart attack. Their presence in the blood can indicate heart damage. However, some of these proteins (CK, CKMB, and myoglobin) are also found in other muscles. Thus, these proteins are not specific to the heart, and elevated levels within the blood can be caused by problems with other muscles in the body.

A newer blood test (designed to detect cardiac troponin) is both more sensitive and more specific for heart damage. Cardiac troponins are found only in the heart. Depending on the hospital, either troponin I or troponin T is measured; in general, both work equally well. Current guidelines recommend that several measurements be obtained over a period of 8 to 12 hours after admission. Because there is a lag from the onset of heart damage to appearance of troponin in the blood, serial monitoring is important to avoid missing a heart attack. Patients with elevated cardiac troponin blood levels have likely suffered heart damage and are at increased cardiac risk. A lack of troponin (or any of the other proteins mentioned above) does not demonstrate an absence of heart disease, only the absence of heart damage. Further testing is necessary after the blood testing to determine if the chest discomfort is a warning sign of a heart attack (see also the Cardiology Patient Page by Ornato and Hand. Warning signs of a heart attack. *Circulation*. 2001;103:e124–125). This testing may occur in the hospital or in your doctor's office.

Another test has been recently released for use in patients who present to the emergency department with chest pain. Ischemia modified albumin (IMA) is indicated for use in patients who are felt by their doctors to possibly be experiencing warning signs of a heart attack (ischemia). This test measures changes that may occur to albumin when ischemia has occurred. The Food and Drug Adminstration has cleared this test for excluding ischemia in patients with negative troponins and normal ECGs. However, patients without evidence of ischemia can also have high levels of IMA. Thus, patients with elevated levels of IMA require further testing to determine whether a problem exists.

Available Blood-Based Tests for Heart Disease

Substance Detected by Blood Test	Patient Symptoms	Indications of Elevations
Cardiac troponins (I and T)	Chest pain or potential heart attack	Injury to the heart
Ischemia modified albumin	Chest pain or potential heart attack	Possible diminished blood flow to the heart
Natriuretic peptides (BNP and pro-BNP)	Shortness of breath; possible heart failure	Probable congestive heart failure
Lipids (cholesterol, HDL, LDL)	Current or future risk of atherosclerosis	Increased risk of atherosclerosis
C-reactive protein	Current or future risk of atherosclerosis	Increased risk of cardiac events
Lipoprotein phospholipase A2	Current or future risk of atherosclerosis	Increased risk of cardiac events

BNP indicates B-type natriuretic peptide; pro-BNP, N-terminal pro–B-type natriuretic peptide; HDL, high-density lipoprotein; and LDL, low-density lipoprotein.

Tests for Heart Failure

Heart failure is one of the leading causes of illness in the United States and the primary reason for hospital admission for patients over 65 years of age. Heart failure is an inability of the heart to pump a sufficient amount of blood to the body. The most common cause is a weakened heart muscle (usually caused by repeated heart attacks). The diagnosis of heart failure is made on the basis of the patient's presentation and confirmatory tests.

New blood tests also assist physicians in the diagnosis of heart failure. These tests measure substances called natriuretic peptides, which are produced in increased amounts by the heart in response to congestive heart failure. These natriuretic peptides assist in the body's response to heart failure by lowering the pressure in the lungs and increasing the flow of urine. Tests for 2 kinds of natriuretic peptides are currently available for the diagnosis of heart failure: BNP (B-type natriuretic peptide) and pro-BNP (N-terminal pro–B-type natriuretic peptide). Blood levels of both of these substances become elevated in patients with congestive heart failure. Physicians most often use these tests to differentiate patients with congestive heart failure from those with lung (pulmonary) problems. Patients without elevations are very unlikely to have a cardiac cause of their shortness of breath. These levels rise and fall rapidly in response to changes in the degree of congestive heart failure. It is hoped that serial measurements of natriuretic peptides over several days will allow physicians to adjust medical therapy for congestive heart failure so that it is more accurate.

Detection of Future Cardiac Risk

Heart attacks and heart failure are usually the end result of blockages forming in the arteries of the heart caused by atherosclerosis. It has been recognized for over 4 decades that elevations in lipids, especially cholesterol, form a potent risk for future heart disease. Measurement of levels of total cholesterol as well as low-density lipoprotein (LDL, also known as "bad cholesterol"), high-density lipoprotein (HDL, also known as "good cholesterol"), and triglycerides are critical for cardiac risk factor management. Attention to diet, exercise, and drug therapy has been shown to improve lipid levels and lower risk. However, approximately one-third of patients who present with heart attacks have normal cholesterol levels. Clearly, in such patients, other factors are responsible.

Attention has been focused on a blood test that measures the level of C-reactive protein (CRP). CRP is a marker for inflammation, and atherosclerosis has an inflammatory component. Patients with elevated levels of CRP have an increased risk for heart attack, stroke, sudden death, and vascular disease. Physicians are beginning to add the measurement of blood CRP levels to other measures of risk to recommend potential options to reduce risk.

The level of CRP has been shown to correlate with future risk as follows:

- CRP level less than 1: lowest risk
- CRP levels of 1 to 3: intermediate risk
- CRP greater than 3: highest risk

There are several non-drug therapy ways to lower CRP, and all patients with elevated levels of CRP should try to incorporate these modifications. These include weight loss, diet, exercise, and smoking cessation. Diabetes can also increase levels of CRP, and patients with elevations of CRP should be tested for diabetes. Some drugs, particularly aspirin and cholesterol-lowering drugs (especially statins), have been shown to decrease CRP levels. Patients with other risk factors and elevations of CRP may have their therapy adjusted to compensate for the CRP elevations. At present, it is not recommended that patients with CRP elevations but no other risk factors be placed on drug therapy; it is not yet known if drug therapy to lower CRP lowers future risk of heart disease (see also the Cardiology Patient Page by Ridker. C-reactive protein: a simple test to help predict risk of heart attack and stroke. *Circulation*. 2003;108:81–85).

Finally, another test (the PLAQ test) has just been released that measures the level of lipoprotein phospholipase A2 (Lp-PLA2). Lp-PLA2 generates oxidized molecules within the blood vessel wall that are more prone to lead to both atherosclerosis and irritability of the atherosclerotic plaque. Elevations in the levels of Lp-PLA2 have been shown to indicate greater risk of plaque formation and rupture independent of the levels of either lipids or CRP. Patients with elevated levels of Lp-PLA2 seem to be at a greater risk of cardiac events. Many of the therapies listed above for the treatment of elevations of CRP are thought likely to also help with elevations of Lp-PLA2.

References

1. American Heart Association. Heart disease and stroke statistics – 2003 update. Available at: http://www.americanheart.org/downloadable/heart/10590179711482003HDSStatsBookREV7-03.pdf. Accessed December 19, 2003.

Additional Resources

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3. Mayo Clinic web site. Available at: http://www.mayoclinic.com. Accessed December 19, 2003.
4. Cleveland Clinic web site. Available at: http://www.clevelandclinic.org. Accessed December 19, 2003.
5. Brigham and Women's Hospital web site. Available at: http://www.brighamandwomens.org. Accessed December 19, 2003.
6. WebMD. Available at: http://www.WebMD.com. Accessed December 19, 2003.