Old Diagnostic Friends Revisited
An Evaluation of Cardiac Enzymes

In 1954, LaDue et al. first noted rises in serum glutamic oxaloacetic transaminase (SGOT) enzyme levels following myocardial infarction. This important observation led to the evaluation of this and other serum enzyme systems as specific and sensitive indicators of myocardial infarction. Elevation of serum creatine phosphokinase (CPK) appeared to be a more sensitive conventional serum enzyme criterion for acute myocardial infarction, but false-positive results occurred frequently. In 1934, Lohman first described CPK which is found in high concentration in striated muscle, cardiac muscle, and brain tissue. Other conventional enzymes have also been used as markers for myocardial infarction, including lactate dehydrogenase (LDH) and hydroxybutyrate dehydrogenase.

Although many of these enzyme assays were fairly sensitive markers for myocardial infarction, they were nonspecific. Levels of SGOT were particularly vulnerable to misinterpretation because SGOT is elevated in patients with hepatocellular disease that may frequently coexist with heart disease. Since CPK levels are elevated in such diverse processes as muscle trauma, skeletal muscle disorders, neurologic disease, hypothyroidism, and pulmonary disease, they are also subject to misinterpretation.

Evaluation of isoenzyme levels of CPK and LDH has offered greater specificity for diagnosing myocardial infarction. Creatine phosphokinase is a dimer composed of M and B subunits. There are three isoenzymes: CPK-MM, CPK-MB, and CPK-BB. Roberts et al. measured total CPK activity and CPK isoenzyme activity in extracts of human skeletal muscle, heart, brain, stomach, small intestine, colon, liver, spleen, lung, kidney, and red blood cells. Substantial amounts of CPK activity occurred only in skeletal muscle, heart, brain, and the gastrointestinal tract. Creatine phosphokinase activity in the lung and kidney was less than 3 percent of that in the myocardium. Of the tissues surveyed, only myocardium was believed to contain significant amounts of CPK-MB isoenzyme. The CPK-MM isoenzyme is found primarily in skeletal muscle and the CPK-BB isoenzyme is found primarily in the brain.

Each of the five LDH isoenzymes is a tetramer composed of varying combinations of H and M subunits. In normal circumstances LDH-2 is more prevalent in the serum than LDH-1. When LDH activity is elevated and the ratio of LDH-1/LDH-2 is greater than 1, there are few diagnostic possibilities other than acute myocardial infarction, acute renal infarction, or hemolysis. An increased and dominant LDH-1 isoenzyme level indicates either hepatic or skeletal muscle injury.

Graeber and associates have performed animal studies that suggest that CPK-MB isoenzyme is also present in the esophagus and small intestine. They have also documented that LDH-1 was found in greater percentage than LDH-2 only in the ventricle of the heart.

In this issue of Chest (see page 521) Graeber and associates present an excellent clinical follow-up of their previous animal studies. Serum enzyme levels of CPK, LDH, and their isoenzymes were followed in three groups of patients: those having an acute myocardial infarction documented by electrocardiographic changes, those suspected of having mesenteric artery ischemia in whom bowel infarction was subsequently documented by surgery or autopsy, and a control group of patients who had elective aorto-iliac peripheral vascular surgery.

In the study they demonstrated that total CPK enzyme levels were elevated in all three groups but CPK-MB isoenzymes were elevated only in the myocardial infarction and the bowel infarction groups. There was no difference in either percent CPK-MB or in total international units of CPK-MB between these two groups of patients. Fortunately, the two groups could be distinguished by examining LDH isoenzymes. The LDH-1/LDH-2 ratio was reversed in the myocardial infarction group and remained normal in the bowel infarction group, allowing a sensitive method for differentiation. Lactate dehydrogenase did not rise significantly in the control vascular surgery group. In addition CPK-BB fractions were mildly elevated in the bowel infarction group of patients but in neither of the other groups.

This report is of clinical importance because mesenteric ischemia and bowel infarction are relatively uncommon and are frequently misdiagnosed as a myocardial infarction. The LDH isoenzymes are more specific for documenting myocardial infarction than elevations of CPK-MB isoenzymes that can occur in patients following median sternotomy, esophageal procedures, and bowel infarction.

Evaluation of both CPK and LDH isoenzyme levels drawn within the first 48 hours of an acute episode of suspected myocardial infarction combines the high degree of sensitivity of CPK-MB determination with the high degree of specificity offered by evaluation of LDH isoenzymes. They should not be evaluated alone. Nowhere is the increased discrimination offered by evaluation of both isoenzymes more important than in evaluating a postoperative surgical patient for a possible myocardial infarction. Following open heart surgery, CPK-MB isoenzyme may be elevated from the median sternostomy incision or from trauma to the atra due to cannulation. In the patient who has...
undergone general surgery, CPK-MB isoenzymes may be elevated if there is vascular compromise or major trauma to the esophagus or intestines. In each case, concomitant evaluation of LDH isoenzymes allows appropriate discrimination from myocardial infarction. This current article by Graeber et al completes a cycle of excellent work that started in the animal laboratory and is herein followed to its clinical conclusion.

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