Serum Enzyme Determinations in the Diagnosis and Assessment of Myocardial Infarction

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Diagnostic Enzymology has grown exponentially since elevated serum amylase was first associated with pancreatitis in 1908 and Karmen, Wroblewski, LaDue, and their associates demonstrated in 1954 that SGOT* and LDH activity in serum increased following myocardial infarction. Following Markert's elucidation of the nature of LDH isoenzymes their importance in differential diagnosis was emphasized. Serum CPK elevations following myocardial infarction were first reported by Dreyfus and his co-workers in 1960, and soon confirmed by Hess and MacDonald. Determination of SGOT, LDH, and CPK activity rapidly became cornerstones in the laboratory diagnosis of acute myocardial infarction in man.

Activity of many enzymes including aldolase, malic dehydrogenase, isomerase, and ICD may increase following myocardial infarction. Serum GGT, a lysosomal enzyme, exhibits increased activity late, reaching a peak within 8 days and returning to normal approximately 1 month following the initial insult. SPK contrary to CPK is not elevated following intramuscular injections, while serum GAPDH elevation may precede increases in conventional enzymes and aid detection of extension of myocardial necrosis. However, since SGOT, LDH, and CPK determinations have become established criteria in the laboratory diagnosis of acute myocardial infarction in man, material to follow will concern those three enzymes primarily.

General Considerations

Meaningful interpretation of serum enzyme determinations should be based upon several considerations:

1. Elevated serum enzyme activity associated with disease is generally assumed to reflect activity of enzyme released from injured tissue. In most conditions, the same enzymes with which an injured organ is richly endowed are those exhibiting elevated activity in serum following organ injury. The time course of depletion of enzyme activity from a damaged organ parallels the time course of increase of activity of the same enzyme in serum following the insult. Following experimental coronary artery occlusion, a significant although small myocardial arteriovenous difference of enzyme activity can be demonstrated. On the other hand, peak elevation of serum enzyme activity may not correlate closely with the magnitude of tissue damage, and some enzymes, such as ICD, which decrease in ischemic myocardium and increase in coronary sinus blood following experimental coronary artery occlusion, may not increase concomitantly in serum. These disparities are reconciled when the rate of disappearance of enzyme activity from serum, the rate of release of enzyme from ischemic

*Abbreviations: SGOT = serum glutamic oxaloacetic transaminase; LDH = lactic dehydrogenase; CPK = creatine phosphokinase; ICD = isocitric dehydrogenase; GGT = gamma-glutamyl transpeptidase; SPK = serum pyruvate kinase; GAPDH = glyceraldehyde phosphate dehydrogenase; OCT = ornithine-carbamyl transferase; SGPT = serum pyruvic transaminase; and NADP = nicotinamide-adenine dinucleotide phosphate.
myocardium, the fraction of myocardial enzyme undergoing local denaturation, and the distribution of enzyme released from the heart in body fluids are taken into account. Thus, ICD activity is not substantially elevated in serum following experimental myocardial infarction because the enzyme's disappearance rate from the circulation is very rapid. Furthermore, when serial changes in serum CPK activity following experimental myocardial infarction are analyzed according to a model based on these considerations, the correlation between myocardial enzyme depletion and increased serum enzyme activity is close \((r = 0.96)\) over a wide range of infarct size.

2. The relative value of enzyme determinations in the diagnosis of a specific disease entity should be assessed on the basis of both specificity and sensitivity of the test. True positives (instances of a positive result in a patient with the disease), false positives (instances of a positive result in a patient without the disease), and false negatives (instances of a negative result in a patient with the disease) should be considered. An enzyme test is highly specific when the ratio of true positives to false positives is high. It is highly sensitive when the ratio of true positives to false negatives is high and the incidence of false negatives is low. Obviously, sampling time and frequency will influence the apparent specificity and sensitivity of the determination.

3. Enzyme determinations are assays of activity, not of amount or concentration of a specific protein in serum. Accordingly, the apparent activity may be influenced by the presence of inhibitors, cofactors, activators, or unusual amounts of substrate or product in the serum sample.

4. The nature of the assay procedure used may influence results profoundly. Since only initial velocity is a reflection of enzyme activity, kinetic assays are generally superior to assays based on a single determination of product concentration and less prone to error introduced by nonspecific chromogens in biologic material.

5. Other factors related to sampling, storage, and laboratory technique may impair the validity of enzyme determinations.

6. The normal range of activity of each serum enzyme must be defined under the assay conditions employed and is usually defined as the mean ± 2 SD of values from a control population. When a skewed distribution is observed in control samples, "normality" may be defined with a log normal curve. These definitions of normality mean that the value obtained in a sample from a normal individual will fall within the normal range 95% of the time. Stated in another way, abnormal values for serum enzyme activity will be obtained in 5% of normal individuals. Thus, an "abnormal" value does not necessarily imply that the patient from whom it was obtained harbors disease.

Enzyme values vary with age, sex, and activity. Accordingly, if a normal range were established based on samples from 18-year-old student nurses, its application to interpretation of values in serum samples from 60-year-old male patients in a coronary care unit would be inappropriate and misleading.

Serum Enzymes in the Diagnosis of Acute Myocardial Infarction

SGOT—Sensitivity and Specificity. In a typical patient with acute myocardial infarction, SGOT activity exceeds the normal range within 8 to 12 hours following the onset of chest pain, reaches a peak elevation of two- to tenfold in 18 to 36 hours, and declines to the normal range within 3 to 4 days. As with all serum enzymes the duration of elevated activity depends in part on the maximum value attained. When other disease processes account for elevated SGOT, the time course often differs. In an extensive review of literature through 1960 by Agress and Kim, 19692 cases of acute transmural myocardial infarction diagnosed clinically and electrocardiographically were tabulated. True-positive SGOT elevations occurred in 97%. Myocardial infarction was proven by autopsy in 119 cases. In 115 of these, SGOT had been abnormal. In
experimental myocardial infarction in animals, SGOT elevations are seen consistently.

SGOT may increase in association with a variety of disease processes, although often the time course of elevated enzyme activity contrasts with that seen typically in patients with acute myocardial infarction. Hepatic congestion, primary liver disease, skeletal muscle disorders, and shock may contribute to marked and sometimes sustained SGOT elevations. In 224 patients with cardiac disease excluding myocardial infarction and shock, SCOT activity was increased in 12%.20 Patients with congestive failure exhibit an even higher proportion of false-positive SGOT elevations apparently in proportion to the severity of failure. However, congestive heart failure in the absence of overt hepatic decompensation is infrequently associated with striking elevations of SGOT.

Myocarditis may lead to SGOT elevations, which frequently parallel the activity of the disorder and are not precluded by steroid administration.21 In pericarditis, SGOT is elevated in less than 15% of patients and those elevations may reflect subepicardial injury.7

Although early reports indicated that SGOT did not generally increase in patients with pulmonary embolism,22 it has become clear that this conclusion is not justified. Coodley noted that four of 17 patients with definite pulmonary embolism and 17 of 25 patients with probable pulmonary embolism manifested increased SGOT activity.23 In other reports, between 25 and 50% of patients with emboli proven angiographically exhibited increased SGOT.24

Increased SGOT activity follows tachyarrhythmia in more than 50% of cases when the heart rate exceeds 140 beats/min for at least 30 min in the absence of acute myocardial infarction. Since OCT is often elevated in such cases,23 the SGOT appears to reflect hepatic decompensation secondary to hemodynamic consequences of the arrhythmia. Accordingly, CPK does not rise nearly as frequently.7 On the other hand, the incidence of arrhythmia within the first 24 hours following myocardial infarction correlates with the magnitude of SGOT elevation26 perhaps because both SGOT and the incidence of arrhythmia reflect the extent of myocardial injury.

Approximately 25% of patients treated with direct-current countershock (electrical cardioversion) may exhibit increased SGOT activity usually less than threefold above normal. Since SGPT and isoenzymes of LDH identified with liver are not elevated in such patients,27 and since OCT, an enzyme identified almost exclusively with liver, does not increase28 it appears that the SGOT rise is due to enzyme release from skeletal muscle. CPK elevations, commonly seen, are both more frequent and more marked than SGOT elevations in this setting.28

Several other conditions, frequently of interest to the cardiologist, may be associated with elevated SGOT activity. Patients with disease of the biliary tract who receive intravenous or intramuscular narcotic injections may exhibit transient increases in SGOT activity.29 Usually, the time course of elevation is much shorter and the magnitude much less than that seen typically following myocardial infarction. Concomitantly increased alkaline phosphatase activity is a valuable confirmatory sign indicating that the enzyme elevation is related to cholestasis potentiated by narcotic administration rather than to myocardial damage.

Approximately 11% of females taking oral contraceptive medication exhibit increased SGOT, usually late in the menstrual cycle,30 and SGOT may be increased in patients treated with clofibrate. SGOT and CPK increased in 8% of 60 patients treated with large doses of clofibrate, and elevated enzyme activity and an associated myalgia waxed and waned with drug administration or its discontinuance, respectively.31 False-positive SGOT elevations following erythromycin administration are a problem only when the colorimetric enzyme assay is employed.32

SGOT may increase following cardiac catheterization. In both adults and children, the magnitude of serum enzyme elevations appears to be related to the duration and extent of dissection required during the procedure.33
Typically, SGOT rises following operation in the experimental animal and in as many as 95% of patients following general surgical procedures. Although increased SGOT may result from hepatic damage by anesthetic agents in some cases, its magnitude appears to depend primarily on the extent of dissection.

Serum enzyme elevations may become clinically important indices of rejection following cardiac transplantation. In a recent experimental study, discrete SGOT and CPK elevations appeared to provide sensitive criteria of incipient rejection in the dog.

LDH—Sensitivity and Specificity. In a typical patient with acute myocardial infarction serum LDH activity exceeds the normal range within 24 to 48 hours, reaches a peak elevation of two- to tenfold in 3 to 6 days, and declines to the normal range within 8 to 14 days. True-positive LDH elevations occurred in 86% of 282 patients with myocardial infarction diagnosed clinically and in all 39 patients with myocardial infarction proven at autopsy. Results in other series are similar.

The specificity of LDH as an index of acute myocardial infarction depends on the population at risk. Increased LDH occurs in 30% of patients with congestive heart failure, and its time course may resemble that following acute myocardial infarction.

Serum LDH activity may increase markedly under the following conditions: hemolysis, in the sample, or in vivo; megaloblastic anemia or anemia associated with ineffective erythropoiesis; leukemia; acute and chronic liver disease; and renal disease, especially renal infarction. Striking serum LDH elevations are seen in many patients with neoplastic disease, and elevations in cerebrospinal, pleural, or ascitic fluid may be indicative of local neoplasm. LDH increases even more commonly than SGOT following pulmonary embolism.

In the dog, increased serum LDH activity is a concomitant of acute pulmonary embolism produced by administration of autologous thrombus despite the absence of pulmonary infarction and underlying heart disease. Many conditions associated with SGOT elevation including cardiac catheterization, myocarditis, and shock may give rise to increased serum LDH activity as well. In addition, LDH may increase following severe exercise apparently because of release of enzyme not only from skeletal muscle but also from liver and myocardium. LDH does not increase as commonly as SGOT following electrical cardioversion, but it may be released from skeletal muscle and/or liver judging by the serum isoenzyme profile seen.

CPK—Sensitivity and Specificity. In a typical patient with acute myocardial infarction, serum CPK activity exceeds the normal range within 6 to 8 hours, reaches a peak of two- to tenfold in 24 hours, and declines to the normal range within 3 to 4 days following the onset of chest pain. The upper limit of normal CPK in females is only about two thirds of that in males. CPK is a sensitive index of acute myocardial infarction, but results vary markedly with the assay technique employed. Both sensitivity and the incidence of false positives increase when thiol activation is used. Nevertheless, such activation is essential to assure reproducibility and prevent rapid decay of CPK activity in serum. Unfortunately, interpretation of CPK results from some studies are clouded by other difficulties including use of the forward instead of the back reaction. When CPK is assayed by the back reaction with thiol activation, the sensitivity of CPK is impressive, of the order of 90% or more. On the other hand, when CPK is assayed by other techniques sensitivity suffers.

As with other enzymes, specificity of CPK elevation as an index of acute myocardial infarction is far from unequivocal. Myocardium, skeletal muscle, brain, and thyroid contain complements of CPK. Because of the paucity of CPK in other parenchymal organs, CPK offered promise as a relatively specific index if cardiac injury. However, serum CPK is markedly increased in most patients with muscular dystrophy, inflammatory disease of muscle, alcohol intoxication with or without delirium tremens, diabetes mellitus with or without ketoacidosis, convulsions, psychosis,
and intramuscular injections, apparently because of muscle release. Serum CPK is rarely affected by renal disease.

Contrary to SGOT and LDH, CPK activity usually remains normal in patients with neoplastic disease. However, X-ray therapy involving the heart consistently produced CPK elevations in serum. CPK did not increase in patients exposed to comparable amounts of radiation (2000–5000 rads within 5 weeks) confined to regions excluding the myocardium but including skeletal muscle.

Serum CPK does not generally increase in patients with uncomplicated congestive heart failure. It may increase with pericarditis, but elevations are rare and those that do occur are usually slight. In myocarditis increased CPK activity often parallels the underlying severity of the inflammatory process.

CPK has been considered an effective discriminant in the differential diagnosis between acute myocardial infarction and acute pulmonary embolism. However, even in early clinical reports, occasional patients with pulmonary embolism exhibited increased serum CPK activity. When CPK activity is assayed with thiol activation, increased activity can be detected frequently. Perkoff focused attention on this in a report of three of seven patients with acute pulmonary embolism who exhibited increased serum CPK activity. CPK activity is demonstrable in lung extracts from man and experimental animals. In experimental pulmonary thromboembolism in dogs, serum CPK activity increases consistently two- to threefold despite only transient and minimal hemodynamic changes and the absence of pulmonary infarction. Thus, modest, transient serum CPK elevations are probably relatively frequent following acute pulmonary embolism.

Although SGOT and LDH elevations following tachyarrhythmia appear to be due to enzyme from liver, recent observations in 12 patients demonstrated increased serum CPK activity suggesting possible myocardial enzyme release. Since tachycardia increases myocardial oxygen consumption and infarct size experimentally, CPK elevations may reflect occurrence of some myocardial necrosis in patients with tachyarrhythmia. Increasing heart rate by means of ventricular pacing in otherwise normal dogs to two and one half times the control rate failed consistently to increase serum CPK activity. However, increasing heart rate from 100 to 180 beats/min augmented infarct size and led to associated elevations in serum CPK in five of six conscious dogs with coronary artery occlusion. Electrical cardioversion produces two- to threefold increases of serum CPK activity in up to 75% of cases.

CPK elevations occur in several other conditions of particular interest to the cardiologist. Selective coronary angiography may increase serum CPK. Following cardiac catheterization the incidence and magnitude of serum CPK elevations appear to depend on the extent of muscle dissection involved in the procedure.

Two- to threefold CPK elevations are frequent following intramuscular injections of narcotics, phenothiazines, barbiturates, antibiotics, diuretics, and analgesics even without overt signs of inflammation. CPK, like other serum enzymes, may increase with severe exercise apparently because of altered properties of cell membranes.

LDH Isoenzymes—Sensitivity and Specificity. LDH isoenzyme determinations have enhanced diagnostic accuracy remarkably. The five common LDH isoenzymes are named in order of rapidity of migration toward the anode in an electrophoretic field. Accordingly, LDH1 is the fastest and LDH3 the slowest in conventional systems. Each isoenzyme is a tetrameric unit composed of four subunits of two possible types. The physical properties of individual isoenzymes are determined by the relative percentages of each type of subunit contained. Extracts of heart contain primarily LDH1, while those from liver or skeletal muscle contain mostly LDH4 and LDH5. Characteristic LDH isoenzyme profiles in specific tissues may be related to the degree of aerobic metabolism typical of the organ. Since LDH1 and LDH2 are susceptible to inhibition.
by pyruvate, this substrate may be preferentially shunted into mitochondria and metabolized aerobically in organs rich in these isoenzymes, such as heart. However, it is not clear that this mechanism operates in vivo, and myocardial LDH profiles may change under altered physiologic states.

Following acute myocardial infarction increased serum LDH1 activity frequently precedes increased total LDH and, in fact, is typically present in the first available blood sample obtained from patients hospitalized for acute myocardial infarction. Since many patients with increased LDH1 exhibit total LDH activity remaining within the normal range, increased LDH1 activity is a more sensitive, early index of acute myocardial infarction than is total LDH. Its sensitivity exceeds 95%.

In most other conditions in which total serum LDH is increased the isoenzyme profile differs considerably from that seen following acute myocardial infarction. While LDH1 is the most prominent serum isoenzyme following infarction, LDH3 is typically increased when congestive failure occurs without infarction. The isoenzyme profile typical of acute myocardial infarction is rarely seen following acute pulmonary embolism usually associated with elevated LDH2 and LDH3 when experimental pulmonary embolism is produced by administration of autologous thrombus, increased activity of LDH3 accounts for most of the elevated total serum LDH activity.

In cardiac patients, hemolysis associated with jet lesions or prosthetic valves frequently leads to increased serum LDH1, LDH2 may increase in patients with muscular dystrophy, since myopathic tissue contains an unusual proportion of LDH1. Furthermore, LDH1 increases in patients with renal disease, especially renal infarction.

The ratio of LDH1 to LDH2 is increased in young females, particularly during pregnancy, compared to postmenopausal females or to males. Furthermore, physical activity of the subject may influence isoenzyme profiles. In well-conditioned males, LDH5 increases following exercise, presumably because of release of enzyme from skeletal muscle. LDH1, LDH2, and LDH3 increase in exercised rats, probably because of release from heart, skeletal muscle, and liver since tissue LDH decreases in all three organs.

Although patients with arrhythmia may exhibit increased total serum LDH activity, the isoenzyme profile is quite different from that seen following acute myocardial damage. Thus, LDH1 activity did not increase in any of 29 patients with tachyarrhythmia. Direct-current countershock may increase total LDH activity because of release of skeletal muscle components, but LDH1 remains normal. LDH1 is usually not elevated in patients with pericarditis, but in approximately 25% of patients with myocarditis LDH1 activity in serum may increase. In patients with heart transplants, rejection episodes are frequently characterized by increased LDH1/LDH2 ratios in serum. Cardiac catheterization, with or without coronary angiography, usually does not lead to significantly increased total or "heart" LDH isoenzyme activity. Thus, LDH isoenzyme analysis may be particularly valuable in assessing the presence or absence of concomitant myocardial infarction in patients with arrhythmia or pericarditis, or those undergoing electrical cardioversion or cardiac catheterization.

Most conditions in which total LDH activity is significantly increased including liver disease, skeletal muscle injury, and shock with skeletal muscle and hepatic ischemia are readily distinguishable from acute myocardial infarction since the isoenzyme profile typically shows predominance of slow components. When coexistent myocardial infarction occurs in patients with these disorders, increased LDH1 may be diagnostically useful in the absence of marked changes in total LDH.

Activities of many serum enzymes are elevated in patients with myxedema. Two mechanisms appear to account for this phenomenon: (1) enzyme release from myopathic muscle, and (2) diminished catabolism of circulating enzyme. The LDH isoenzyme pattern seen in serum from patients with...
myxedema typically exhibits elevated LDH$_4$ and LDH$_5$. Thus, the pattern is readily distinguishable from that seen with ischemic myocardial injury.

Efforts directed toward detecting "heart" LDH isoenzymes by rapid chemical procedures rather than electrophoretic techniques exploit properties of the dominant LDH subunit seen in heart LDH isoenzymes including heat stability, susceptibility to inhibition by pyruvate, resistance to inhibition by urea, and affinity for alpha-hydroxybutyric acid as a substrate. Alpha-hydroxybutyric dehydrogenase (α-HBD) should not be viewed as a specific enzyme but rather as enzymatic activity residing in that fraction of LDH with high affinity for alpha-hydroxybutyric acid.

Electrophoretic analysis of LDH isoenzymes continues to provide a more-sensitive and specific diagnostic index compared to the chemical techniques. However, precautions required include assay of enzyme activity within the range of linearity of the staining procedure used and control of temperature throughout the supporting medium. The major difficulty with chemical methods is that specific isoenzymes are not identified. Apparent enzyme activity with the chemical methods depends on total LDH activity and total subunits of each type rather than the isoenzyme profile per se. Thus, chemical inhibition methods may fail when total LDH activity is high. Lack of agreement between results of "heart" LDH isoenzyme activity estimated by urea inhibition and that determined electrophoretically occurs in as many as 24% of samples, with frank contradiction in as many as 10%. Despite these qualifications, LDH fractionation by chemical techniques led to true-positive results in a combined total of 457 of 464 patients from several centers. Thus, results with chemical fractionation techniques are more specific and sensitive than total LDH determinations, while those obtained with isoenzyme separation by electrophoresis surpass both.

Activity of Serum Enzymes in Patients with Coronary Insufficiency

Insufficient coronary blood flow may be associated with several clinical syndromes and pathologic consequences. Yet, elucidation of the relationships between each of these syndromes and changes in serum enzymes has been difficult. In order to examine these relationships, it is useful to consider four syndromes of apparently decreasing severity: (1) definite transmural myocardial infarction with evolution of Q waves; (2) prolonged chest pain due to myocardial ischemia and associated with transient S-T-segment and T-wave changes; (3) prolonged chest pain due to ischemia but associated with no electrocardiographic changes; and (4) typical angina pectoris. Compilation of data from several studies indicates that 92, 58, 27, and 5% of patients in these four categories, respectively, exhibit elevated SGOT, CPK, LDH, and/or LDH$_4$.4, 7, 8, 10, 16, 17, 19, 46, 60, 61, 63–65

Several conclusions appear warranted. The incidence and extent of enzyme elevations vary widely in patients with insufficient coronary blood flow without transmural myocardial infarction, probably because criteria for patient classification vary. The incidence of increased serum enzyme activity is greatest in patients with transmural myocardial infarction, decreases in those with chest pain and associated electrocardiographic changes, and is least in those with prolonged chest pain or angina pectoris without any electrocardiographic changes. This trend is consistent with the possibility that prevalence of myocardial necrosis in these patient groups follows the same trend and that enzyme elevations reflect necrosis.

Enzyme elevations that do occur are modest in patients with insufficient coronary blood flow without transmural myocardial infarction. Mortality following definite myocardial infarction parallels, in general, the magnitude of peak enzyme elevation acutely. Thus, available clinical data are consistent with the interpretation that serum enzyme elevations following myocardial ischemia are indicative of myocardial necrosis.
Clearly, the wide spectrum of necrosis seen clinically may include massive infarction on the one hand, and miniscule islands of myocardial-cell death on the other, with profoundly different prognostic and therapeutic implications.

Quantitative Relationships between the Extent of Myocardial Necrosis and Changes in Serum Enzymes

In unselected patients with acute infarction when SGOT, LDH, and/or CPK activity increases more than tenfold, mortality rises markedly. This correlation may result from a general dependence of both mortality and peak enzyme activity on the extent of myocardial necrosis. In one large autopsy series, infarcts were graded as small, medium, and large by morphologic criteria. The median peak SGOT and LDH values in patients falling into these respective groups increased correspondingly. Infarct size is large in patients dying with cardiogenic shock associated with myocardial infarction. Under certain circumstances inflammatory or regenerative responses within a damaged organ may increase serum enzyme activity beyond that anticipated from the amount of enzyme initially present in the entire damaged organ. However, this phenomenon does not appear to occur with myocardial damage.

Although peak serum enzyme activity correlates with infarct size in groups of animals despite imprecision in anatomic criteria leading to scatter, the correlation may not be close in the same animal. In order to elucidate the basis of this apparent disparity, we have studied serum and myocardial CPK activity following experimental myocardial infarction. CPK was chosen because this enzyme is not present to a significant extent in cells participating in the inflammatory response in myocardium. In initial studies in rabbits, depletion of myocardial CPK correlated closely with infarct size assessed morphologically 24 hours after coronary artery occlusion. CPK depletion in selected regions from dog hearts 24 hours after coronary artery occlusion correlated closely with the extent of acute cellular injury in the same site measured independently with the use of epicardial electrocardiographic recordings. A method based solely on serial changes of serum CPK activity was then developed for quantitative assessment of infarct size in the conscious animal. CPK released from the infarct was determined solely on the basis of serial serum CPK measurements analyzed with a model accounting for the rate of CPK disappearance from serum, the rate of release of CPK from myocardium undergoing infarction, the fraction of myocardial CPK degraded locally in the heart, and the distribution space into which CPK is diluted following release into the circulation, all of which were determined independently. Infarct size calculated on the basis of observed changes in serum CPK activity was compared with infarct size determined directly by analysis of myocardial CPK depletion in 22 animals. The correlation was close in each case. Results from all experiments fit a regression line with narrow confidence limits and a correlation coefficient of 0.96. These findings are consistent with the bulk of earlier experimental work and clinical observations that support the hypothesis that elevation of serum enzyme activity following myocardial infarction is a reflection of enzyme release from myocardial cells undergoing necrosis. Thus, although the relationship between changes in serum enzyme activity and infarct size is complex it appears to be quantitative. Accordingly, analysis of changes in serum enzyme activity following myocardial infarction should permit the accurate assessment of the extent of myocardial necrosis and its progression, so that the potent surgical tools becoming available for the patient with coronary artery disease can be focused effectively.

Conclusions

SGOT, LDH, CPK, and LDH isoenzyme determinations are of immense value in the assessment of patients with coronary artery
disease. Meaningful interpretation of such determinations requires knowledge of sampling technique, assay conditions, and physiologic and pathologic states capable of influencing serum enzyme activity. The time course, magnitude, and pattern of serial changes are helpful in identifying responsible etiologic factors. Following acute myocardial infarction, serum LDH1, CPK, and SCOT rise promptly. Total LDH activity increases later and appears to be a somewhat less-sensitive index. All enzymes suffer from some lack of specificity. Total LDH and LDH1 are particularly prone to spurious elevations when hemolysis is present in vivo or in vitro. LDH1 and CPK are less likely than SGOT and total LDH to increase in patients with congestive heart failure. LDH1 is particularly useful in differentiating acute myocardial infarction from acute pulmonary embolism and in excluding myocardial injury in patients treated with direct-current countershock or studied invasively in whom serum activity of SGOT, CPK, and LDH derived from skeletal muscle may increase. Extensive evidence supports the conclusion that serum enzyme elevations following myocardial ischemia are related quantitatively to enzyme release from irreversibly injured cells. Continued elucidation of changes in serum enzyme activity should be of considerable practical value in detecting and assessing the extent of infarction and its progression in individual patients with coronary artery disease.

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_Circulation_. 1972;45:471-482
doi: 10.1161/01.CIR.45.2.471

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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