# SERUM TRANSAMINASE DETERMINATIONS AS A DIAGNOSTIC AID IN MYOCARDIAL INFARCTION

BY

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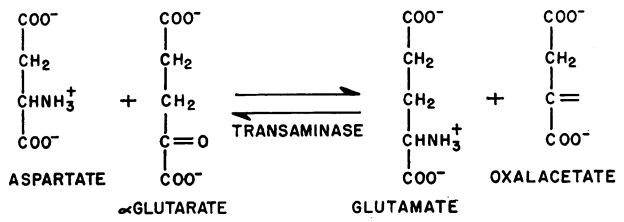
In 1955 La Due and Wróblewski observed that the serum level of glutamic oxalacetic transaminase (transaminase) activity rises after acute myocardial infarction. Thus to the well-established criteria of clinical history and examination, together with the changes in the electrocardiogram, blood sedimentation rate, white-cell count, temperature chart, and urobilinogen excretion, a new biochemical test has been added which helps to determine whether or not recent myocardial infarction has occurred. Since that time several other reports describing increased serum transaminase activity following myocardial infarction have been published (Chinsky *et al.*, 1956; Kattus *et al.*, 1956; Merrill *et al.*, 1956).

Transaminase is present in many mammalian tissues and was found by Cohen and Hekhuis (1941) to be particularly abundant in cardiac and skeletal muscle. Brain, liver, and kidney follow muscle in decreasing order in transaminase content (La Due *et al.*, 1954). These authors define transamination as the enzymatic catalysed reversible transfer of the alpha-amino-nitrogen of an amino-acid to the alpha-keto-acid, with the synthesis of a second amino-acid and a second alpha-keto-acid.

The transaminase reaction—which may be written thus—




is coupled *in vitro* to a second reaction, the reduction of the oxalacetate (produced in the transamination reaction) to malate by reduced diphosphopyridine nucleotide (D.P.N.H.). The light absorption peak of D.P.N.H. at 340 mμ is used to measure the transamination reaction spectrophotometrically by observing the decrease in light absorption at that wavelength as D.P.N.H. is oxidized. The Beckman D.U. model spectrophotometer is employed. In this study the details of the method described by Karmen *et al.* (1955) have been followed. Transaminase activity is expressed as units per ml. of serum per minute. One unit equals a decrease in optical density of 0.001.

Nydick *et al.* (1955) produced experimental myocardial infarctions in dogs. They demonstrated that the enzyme activity of infarcted muscle is reduced to 2–10% of that of normal cardiac tissue, and they conclude that serum transaminase activity increases significantly following myocardial infarction because transaminase is released into the blood stream as a result of an increase in the permeability of the injured heart-muscle cells. They also showed that ischaemia of 45 minutes' duration failed significantly to influence the transaminase activity. It follows that increased activity may be predicted only in the presence of tissue destruction and not where ischaemia has been insufficient to cause necrosis. There have also been reports on transaminase levels in liver disorders and other conditions (Chinsky *et al.*, 1956; Wróblewski and La Due, 1956).

### Present Investigation

The present study has been limited to the application of the test to patients with coronary sclerosis. Twenty patients were studied in order to determine the normal range of serum transaminase activity in our laboratory. Six of these attended the long-term anticoagulant clinic, and none of them was suspected of a recent thrombo-embolic incident. They all had serum transaminase values within the normal range of previous workers—that is, 10–40 units.

A group of five random post-operative patients was also studied. Each had undergone operation within the 24 hours preceding transaminase determination. All except one showed results within the normal range. This patient had had cholecystectomy for obstruction of the common bile duct and showed evidence of jaundice and impaired liver function. In her the level was raised to 64 units.

A further random group of nine were medical in-patients without evidence of recent myocardial infarction. The results in all but one were within the normal range. The one exception was an elderly man admitted with haematemesis. His electrocardiogram was abnormal, and although not diagnostic did not exclude myocardial infarction. He underwent partial gastrectomy and died a few days later. Post-mortem examination revealed that there was a small recent myocardial infarction. The pathologist reported that its age was consistent with the occlusion having occurred shortly before the specimen for transaminase determination was drawn.

Normal values were thus obtained in 18 control patients, including four who had had operations within the previous 24 hours. In two patients abnormal values were obtained, but one of these had liver disease and the other was eventually shown to have suffered acute myocardial infarction.

Determinations were made on an additional group of 39 patients who were suspected of coronary artery disease. In 13 of the 39 the clinical and electrocardiographic findings were typical of acute myocardial infarction. Of this group all but one had increased serum transaminase activity (Table I). The exception was a patient whose only sample was drawn two hours after the onset of pain, and who died before further samples were obtained. Necropsy revealed a massive posterior myocardial infarction.

In 4 of the 39 cases the electrocardiograms made upon admission to the hospital were not helpful in diagnosing or excluding the presence of acute myocardial infarction. In two of these the clinical findings also were atypical. In all patients of this group a final diagnosis of acute myocardial infarction was eventually made after several days by a critical survey of the clinical and electrocardiographic course. The results in this group are shown in Table II, from which it is seen that positive transaminase levels were found in all.

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TABLE I.—*Serial Serum Transaminase Activity in Patients With Typical Myocardial Infarction*

| Case No. | Time After Clinical Onset | | | | |
|---|---|---|---|---|---|
| | 0–10 Hrs. (Units) | 10–24 Hrs. (Units) | 48 Hrs. (Units) | 96 Hrs. (Units) | 1 Week (Units) |
| 1 | 20 | 196 | 248 | 60 | 31 |
| 3 | 6 | — | — | — | — |
| 5 | 32 | 144 | 42 | 36 | 33 |
| 6 | 22 | 64 | 83 | 41 | 32 |
| 10 | 39 | 206 | 25 | 33 | 26 |
| 11 | 26 | 75 | 103 | 44 | — |
| 15 | 19 | 270 | 196 | 61 | 44 |
| 17 | 92 | 116 | 45 | 21 | 17 |
| 19 | 47 | 60 | 34 | — | 8 |
| 25 | — | — | 86 | — | — |
| 33 | 21 | 166 | 101 | 28 | 16 |
| 35 | 12 | 68 | 34 | — | 18 |
| 36 | 24 | — | 62 | 32 | 22 |

TABLE II.—*Serial Serum Transaminase Activity in Patients With Myocardial Infarction Presenting Diagnostic Difficulty*

| Case No. | Time After Clinical Onset | | | | |
|---|---|---|---|---|---|
| | 0–10 Hrs. (Units) | 10–24 Hrs. (Units) | 48 Hrs. (Units) | 96 Hrs. (Units) | 1 Week (Units) |
| 2 | — | 59 | 58 | 27 | 26 |
| 9 | 39 | 101 | 51 | 26 | 27 |
| 13 | — | — | 50 | 39 | 18 |
| 39 | — | — | 60 | 22 | 33 |

In Case 9 serial electrocardiograms over a period of a month never showed a pattern diagnostic of myocardial infarction, but in this patient the clinical history and subsequent course were in every way typical.

In Case 2 the patient was a 76-year-old woman with chronic lung disease who was admitted with acute pulmonary oedema and whose electrocardiogram on admission showed complete right bundle-branch block. There were marked ST–T shifts, but it was not possible to tell whether these were primary and due to developing infarction or whether they were merely secondary to the large QRS complexes. Inspection of serial records made over a period of a week revealed changes in the shape and deflection of the ST–T segments and allowed of a retrospective diagnosis of myocardial infarction.

In Case 13 the patient had been suffering from prolonged anginal attacks, and the onset of infarction was impossible to date. It was not until several days after admission that a high postero-lateral infarction pattern was demonstrated on her electrocardiogram.

Case 39 was clinically in every way typical, but T-wave inversions were the only electrocardiographic abnormalities demonstrable in serial records.

Twelve patients on admission to hospital were suspected on clinical and electrocardiographic grounds of having sustained acute myocardial infarction. Follow-up did not substantiate the diagnosis in any patient in this group. The negative results of serum transaminase determinations, together with the diagnosis upon discharge, are shown in Table III. The results of transaminase determinations were not taken into consideration by the physicians making the final diagnoses.

TABLE III.—*Serial Serum Transaminase Activities in Patients Initially Suspected of Myocardial Infarction*

| Case No. | Time After Clinical Onset | | | | | Final Diagnosis |
|---|---|---|---|---|---|---|
| | 0–10 Hrs. (Units) | 10–24 Hrs. (Units) | 48 Hrs. (Units) | 96 Hrs. (Units) | 1 Week (Units) | |
| 4 | 15 | 23 | 22 | 30 | 26 | Hydrops of gall-bladder |
| 7 | 27 | 26 | 16 | 15 | 21 | Angina pectoris |
| 8 | — | 23 | 24 | 36 | 19 | Coronary insufficiency |
| 12 | — | 13 | 26 | 22 | — | Angina pectoris |
| 16 | — | 8 | 16 | 15 | 12 | Angina pectoris. Marked superimposed neurosis |
| 18 | — | 19 | 22 | 22 | 18 | Residua from thoracic injury |
| 20 | — | 23<br>34 | 26<br>— | 38<br>21 | — | Two severe attacks of coronary insufficiency one month apart |
| 27 | — | 12 | — | — | — | Bronchitis |
| 28 | — | — | 12 | 14 | — | Coronary insufficiency, probable. Definite diagnosis not established |
| 29 | — | 35 | — | 18 | — | Coronary insufficiency |
| 32 | 40 | 28 | 20 | 12 | 14 | Severe coronary insufficiency. Marked hypercholesterolaemia |
| 37 | — | 14 | 14 | 14 | 17 | Coronary insufficiency |

In Case 4 a 63-year-old man had complained for some months of pain in the chest and was admitted complaining of severe xiphisternal and epigastric pain. He had had previous electrocardiograms showing complete right bundle-branch block. The electrocardiogram made on admission was similar, except that there was depression of ST–T in lead aVF. A provisional diagnosis of posterior myocardial infarction was made, and it was not until a week after the onset that a large palpable mass in the right upper abdominal quadrant betrayed the diagnosis of hydrops of the gall-bladder.

In Case 18 the patient was a 35-year-old man who one year previously had sustained a steering-wheel accident, with injury to his sternum and with the development of an acute antero-septal myocardial infarction pattern in an electrocardiogram recorded immediately after the accident. He was admitted to hospital complaining of severe precordial pain of one hour's duration, and his electrocardiogram showed ST–T elevations in leads V2, V3, and V4, and Q waves in leads V5 and V6. No change was observed in serial records made over a three-weeks period.

In Case 32 the patient was a 39-year-old woman with profound coronary insufficiency and hypercholesterolaemia. An infarction pattern was not observed on any of several electrocardiograms. No sample of serum showed abnormally elevated transaminase activity, but the falling titre from the upper toward the lower limit of the normal range suggested the possibility that minimal infarction may in fact have occurred.

Single specimens from six patients with classical angina pectoris were drawn on a day in which there had been at least one attack. The results are shown in Table IV. All were negative.

TABLE IV.—*Serum Transaminase Activity in Patients With Severe Angina Pectoris*

| Case No. | 23 | 24 | 30 | 31 | 34 | 38 |
|---|---|---|---|---|---|---|
| Result in units .. | 16 | 9 | 14 | 20 | 16 | 14 |

Raised serum transaminase activity was demonstrated in a patient with intractable cardiac failure and a very large congested liver (44 units), in a patient with cirrhosis of the liver and ascites (72 units), and in a patient with acute pancreatitis (serum amylase 1,600 units, serum transaminase 238 units).

One patient, a 65-year-old man with arteriosclerotic heart disease, was admitted with shock, pulmonary oedema, and cold, pale, pulseless lower extremities. A diagnosis of saddle embolus of the aorta and possible complicating myocardial infarction was made, but the transaminase determination on a sample drawn 15 hours after the onset was negative (8 units). He died 48 hours after the onset, and permission for necropsy was refused. The negative result was unexpected, as Merrill *et al.* (1956) recorded high levels in two patients, one with a saddle embolus at the aortic bifurcation and the other with severe diabetic gangrene of the lower extremities.

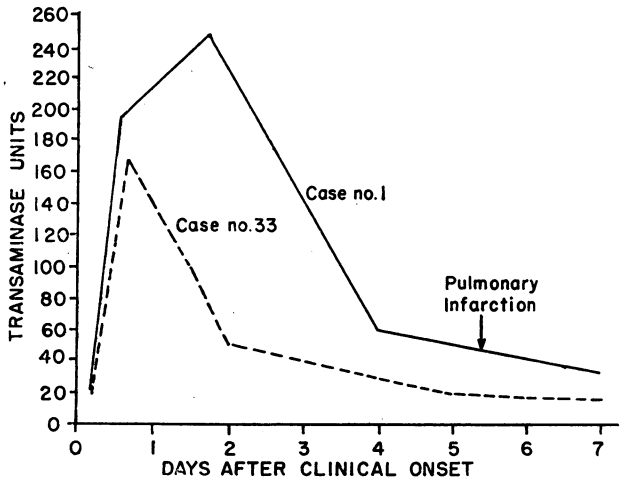
## Discussion

The discovery of a test useful in the recognition of myocardial infarction and the extraordinarily high incidence of coronary sclerosis among the patients admitted to a private hospital in a busy American city prompted us to test the value of the method on our own patients and in our own laboratory and to report our results.

No "false positives" or "false negatives" were recorded. The test found its greatest application where myocardial

infarction was suspected, but could not be proved, and in cases where infarction was not strongly suspected but had to be excluded.

In myocardial infarction the peak values of heightened activity occurred early, being found 12 to 24 hours after the clinical onset. Normal values were found in samples taken within the first few hours following the onset of pain. Values were again normal in samples withdrawn five to eight days following myocardial infarction. The Chart illustrates the curve obtained in two typical cases when the serum transaminase is plotted against time. These time relationships agree closely with those reported by La Due and Wróblewski (1955) and by Kattus *et al.* (1956).




Curves for two typical cases.

The test is most useful in myocardial infarction if a sample can be obtained within a few hours after the onset. Such a sample will show a normal transaminase. One and preferably more samples should be obtained over the ensuing 36 hours to demonstrate high levels and a final sample tested a week after infarction to demonstrate return to normal levels.

Liver and renal disease are unlikely to cause confusion, since they can be differentiated on clinical grounds. Furthermore, Wróblewski and La Due (1956) have shown that, as would be expected in these conditions, abnormal values persist not for a few days but over prolonged periods. Acute pancreatitis may be responsible for very high levels, as in our own case and in the cases of Chinsky *et al.* (1956). Unfortunately, therefore, the test is of no value in making the important differential diagnosis of this condition from myocardial infarction.

Our results suggest that a major surgical operation does not cause enough muscle damage to influence the serum transaminase activity. This observation may be helpful in cases where sudden collapse following operation has occurred and the transaminase test is employed to help determine whether or not the cause is acute myocardial infarction. We have not as yet studied a large post-operative group with serial determinations.

The persistently negative results recorded in patients with angina pectoris of greater or lesser severity, especially where interpretation of the electrocardiogram is difficult because of previous infarctions or left bundle-branch block or arrhythmia, is particularly helpful for the exclusion of acute myocardial infarction.

Case 1 was complicated by a pulmonary infarction on the fifth day following myocardial infarction. This event did not disturb the smooth descent of the transaminase to normal. A rise in serum transaminase was not to be anticipated, since Agress *et al.* (1956) produced massive infarction experimentally in dog lungs without a significant rise in their serum transaminase activity.


## Summary

Serial serum transaminase activity determinations were made on 39 patients. Abnormally high levels were recorded in 16 out of 17 cases of acute myocardial infarction. One patient did not survive long enough for serial samples to be obtained. Four patients in this group were clinically atypical.

Normal values were obtained from 12 patients who were suspected of having acute myocardial infarction at the time of their admission to hospital but whose subsequent courses negated this diagnosis. Most of these patients were the subjects of coronary sclerosis.

In six cases of classical angina pectoris the serum transaminase activity was normal.

In one patient with acute pancreatitis the level was very high.

Serial serum transaminase determinations serve as a useful test in distinguishing cardiac pain caused by ischaemia alone from that in which necrosis of myocardial cells has occurred.

The time relationships found by previous workers are confirmed. Normal levels may be anticipated during the first 6 to 10 hours; thereafter, and up to the third day, abnormally high values are found. The peak level usually occurs between 12 and 24 hours after infarction. High levels sometimes persist into the fourth day. Serum transaminase activity returns to normal within a week from clinical onset of pain. The importance of obtaining early samples is evident.

Liver disorders and conditions other than coronary sclerosis were not studied.

Recent surgical operation did not interfere with transaminase levels.


We are grateful to all physicians referring cases for this study. We gladly acknowledge the courtesy of Dr. H. Schiro, Director of the Department of Internal Medicine, Jewish Hospital, Cincinnati, in allowing us to study patients under his care and to publish this report.

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"We intend to use every legal means within our power to protect consumers from being victimized by this worthless treatment," states the U.S. Commissioner of Food and Drugs, Mr. G. P. LARRICK, in a statement on the Hoxsey cancer treatment. The statement was issued by the Federal Department of Health, Education, and Welfare. "For the second time," continues Mr. Larrick, "a Federal court has determined that the Hoxsey medicines for internal cancer are worthless. On November 15, 1956, after a six-week trial in the Federal court at Pittsburgh, the jury returned a verdict that these medicines, in pill form, were illegally offered as an effective treatment for cancer. On November 16 U.S. District Judge JOHN L. MILLER signed an order of condemnation stating that the pills were misbranded as charged by the Government and ordering their destruction."