The Significance of the Serum Glutamic Oxalacetic Transaminase Activity Following Acute Myocardial Infarction

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The serum glutamic oxalacetic transaminase rose two to 20 times normal in 74 of 75 patients who had acute transmural myocardial infarction. The height of the enzymatic activity was roughly proportional to the size of the infarct. Serum glutamic oxalacetic transaminase is unaffected by angina pectoris, coronary insufficiency, heart failure, or digitalis in the absence of active heart cell injury. Experimental myocardial infarction is followed consistently by a two to twenty-fold increase in serum glutamic oxalacetic transaminase activity. Increase in the serum activity of this enzyme appears to be a useful index of the presence of active heart muscle injury.

Serum glutamic oxalacetic transaminase (SGO-T) is widely distributed in animal tissues but is most concentrated in heart muscle. This property led us to study its concentration in human serum following acute myocardial infarction. Serum glutamic oxalacetic transaminase permits the enzyme catalyzed irreversible transfer of the alpha amino nitrogen of aspartic acid to alpha ketoglutaric acid with the synthesis of glutamic and oxalacetic acids as shown in figure 1. Table 1 indicates the relative rate of transamination by heart muscle, skeletal muscle, brain, liver, kidney, testis and lung.

Earlier studies employing paper chromatography demonstrated that glutamic oxalacetic transaminase was present in normal human serum. The enzymatic activity was shown to be stable in serum stored at 0 to 5°C, for periods of up to two weeks and neither freezing nor lyophilization appreciably altered the transaminase activity. The level of serum glutamic oxalacetic transaminase in normal individuals is essentially the same from day to day and remains unchanged in sera stored at 0 to 5°C, for at least two weeks. Heating the sera to 100°C will destroy the activity. Table 2 compares the activity of the serum glutamic oxalacetic transaminase determined by paper chromatography with that obtained by the spectrophotometric method. The values are strikingly similar. A unit of activity is defined as a decrease in optical density of 0.001 μu per milliliter of serum per minute under the conditions described. Glutamic oxalacetic transaminase activity has been demonstrated in all suitably processed sera. The concentration is the same in serum and plasma but is 10 times greater in hemolyzed red blood cells.

Normally the serum glutamic oxalacetic transaminase varies from 10 to 40 units per milliliter when tested at room temperature. Levels above this were not seen in patients with infectious, neoplastic, metabolic, or degenerative diseases in which acute destruction of heart, skeletal muscle or liver tissue could be excluded. There is a strikingly progressive increase in serum glutamic oxalacetic transaminase activity after death which is proportional to the expired time.

Lyophilized coded sera from dogs subjected to acute myocardial infarction in Los Angeles in the laboratory of, and by the technique developed by, Agress, Glassner, and Clark at the Veterans’ Administration Center were tested blindly in New York in our laboratory for serum glutamic oxalacetic transaminase. Figure 2 summarizes the values obtained in animals which at postmortem examination were estimated to have 50 per cent, 20 per cent, and 5 to 10 per cent of their hearts infarcted. Figure 3 presents the same data, plotting the
SERUM GLUTAMIC OXALACETIC TRANSAMINASE ACTIVITY

TABLE 1.—Rate of Transamination for Various Types of Rat Tissue in Microliters per Milligram of dry Weight per Hour and in Micromoles per Gram of Fresh Tissue per Hour

<table>
<thead>
<tr>
<th>TISSUE</th>
<th>MICROMOLE ACTIVITY</th>
<th>MICROLITERS</th>
</tr>
</thead>
<tbody>
<tr>
<td>HEART</td>
<td>3.0</td>
<td>330</td>
</tr>
<tr>
<td>SKELETAL MUSCLE</td>
<td>3.1</td>
<td>289</td>
</tr>
<tr>
<td>BRAIN</td>
<td>3.4</td>
<td>250</td>
</tr>
<tr>
<td>LUNG</td>
<td>3.4</td>
<td>269</td>
</tr>
<tr>
<td>TESTIS</td>
<td>3.5</td>
<td>126</td>
</tr>
<tr>
<td>LIVER</td>
<td>3.6</td>
<td>250</td>
</tr>
</tbody>
</table>

---FROM P. P. COHEN, J.B.C. 130:711 (1940)
---FROM J. ANAPARA, J.B.C. 134:497 (1955)

peak serum glutamic oxalacetic transaminase levels versus the size of the estimated infarct. The data show that the height of the enzyme in the serum following myocardial infarction, is, under the conditions of these experiments, proportional to the size of the infarction. Similar results have been found in dogs whose coronary arteries were ligated at varying levels, the degree of infarction being proportional to the height of the serum glutamic oxalacetic transaminase activity.

FINDINGS IN HUMAN SUBJECTS

The sera of 50 patients who had unequivocal transmural myocardial infarctions were analyzed for serum glutamic oxalacetic transaminase activity at varying times during the first three to 30 days following the onset of chest pain. The sera of 17 of these patients were coded and sent refrigerated from Syracuse University through the courtesy of Dr. Richard Lyons and were analyzed in our laboratory. The serum glutamic oxalacetic transaminase activity was correlated with the clinical course much later. Characteristic serum glutamic oxalacetic transaminase curves with time were obtained in every instance save one. The fact

FIG. 2. Compares the level of the serum glutamic oxalacetic transaminase at varying periods following infarction of 50 per cent, 20 per cent and 10 per cent of dog hearts.
that this serum was drawn on the third day after the onset of pain and was then stored for 21 days prior to analysis may in part explain the discrepancy. It is also possible that infarction occurred two or three days prior to the onset of chest pain.

Figure 4 describes the serum glutamic oxalacetic transaminase activity in a 60 year old white man who developed crushing substernal pain at time zero associated with shock, mild heart failure, and classical electrocardiographic evidence of a large posterior infarct. The serum glutamic oxalacetic transaminase was within normal limits three hours post injury but rose to 500 units within 12 hours, falling off gradually to normal by the sixth day. Figure 5 describes similar serum glutamic oxalacetic transaminase changes in a 36 year old white man with levels of 160 units six hours after the onset of his pain, rising to 430 within 24 hours and falling to 90 by the third day at which time the patient again complained of substernal pain associated with shock. The serum glutamic oxalacetic transaminase levels were 215 on the following day, falling to normal six days later. Note the lack of correlation with the sedimentation rate and white blood count.

We have studied four additional patients who have developed secondary serum glutamic oxalacetic transaminase elevations sometimes associated with pain but always clinically compatible with extension of previous infarction.

Figure 6 summarizes the serum glutamic oxalacetic transaminase activity on various days post injury in 50 patients with transmural myocardial infarction. The horizontal line indicates the level for the number of patients from which the average was computed and the bottom and top of the vertical lines represent the low and high values in the sera tested on the indicated day. By the third day 10 patients had serum glutamic oxalacetic transaminase levels of 49 or less, by the fourth day 17 patients, by the fifth 21, by the sixth 26, and all the rest were below 40 units by the seventh day unless evidence of further infarction developed. Two patients with levels of 5000 and 6000 units on the second day, proven at autopsy to have large myocardial infarctions, were not used in computing the data for this chart, which is representative of the average observations. Both of these patients also had active liver
disease which we have found results in marked elevations of the serum glutamic oxalacetic transaminase. In one instance the serum glutamic oxalacetic transaminase was 1040 by the third day and in the other it remained elevated until death on the third day. Autopsy showed extensive anterolateral infarction and liver necrosis. Both patients were oliguric until death. These data suggest that serum glutamic oxalacetic transaminase is destroyed or changed in the liver, although renal block of excretion cannot be excluded.

The number of patients studied is relatively small, but we were unable to find any correlation between the height of the serum glutamic oxalacetic transaminase and the following clinical observations: age, sex, color, weight, height of temperature, level of the white blood count, the sedimentation rate, the presence or absence of shock, the absolute levels of the blood pressure, the presence of heart failure, the location of the infarction, the mortality rate, or the use of anticoagulant drugs. There was a significant correlation, however, between the serum glutamic oxalacetic transaminase level and the electrocardiographically estimated size of the infarct (the higher the enzymatic activity, the larger the infarct).

Serum glutamic oxalacetic transaminase levels have been determined in a wide spectrum of disease states and have not been found elevated in heart disease except that associated with active myocardial damage. In particular the values have been within normal limits in many patients with angina pectoris and coronary insufficiency even when the latter has been associated with the negative T-wave changes of ischemia. Serum glutamic oxalacetic transaminase has been normal following shock, heart failure, the use of cardiotoxic drugs, cortisone, acute phlebitis, and cerebrovascular damage. It has been found elevated following acute myocardial damage, acute liver injury and following skeletal muscle damage after injury or surgery, after myositis including dermatomyositis, or arterial occlusion. The curve following acute myocardial infarction, however, has not been mimicked by any of the above disease states.

Serum glutamic oxalacetic transaminase rises precipitously following experimentally produced carbon tetrachloride liver damage. Liver cell injury in clinical carbon tetrachloride poisoning, in acute hepatitis, or in homologous serum hepatitis, is also associated with serum
glutamic oxalacetic levels of from 1000 to 12,000 units. Such marked elevations last for a few days but moderate enzymatic activity may persist for two or more weeks before falling to normal. In any event, the curve does not resemble that usually seen after acute infarction of heart muscle.*

**Discussion**

The level of serum glutamic oxalacetic transaminase following experimentally produced myocardial infarction almost invariably rises within four to six hours of injection and remains elevated for from two to five days depending upon the extent of necrosis. The height of the serum glutamic oxalacetic transaminase is roughly proportional to the size of the infarct. This is true whether the infarction results from injection of plastic spheres into the internal carotid, whether it is produced by ligation of coronary arteries in the closed chest or whether the muscle necrosis results from intravenous injection of papain.1, 6, 8

In addition to the 50 patients reported here in detail we have analyzed the serum of another 25 patients with transmural infarction and have found the serum glutamic oxalacetic transaminase elevations of from 70 to 600 units within 12 hours to 6 days post injury in every patient. In 30 instances the analyses were on coded sera thus excluding the chance of predetermination. The single patient who failed to show an increase of enzymatic activity after infarction has already been discussed. Figure 7 shows that the higher the enzymatic activity is, the longer such elevation persists. Since in dogs the height and duration of serum glutamic oxalacetic transaminase activity was proportional to the size of the infarct, we believe a similar finding in humans indicates at least a rough correlation between the amount of muscle necrosis in human myocardial infarction and the level of the serum glutamic oxalacetic transaminase.

Thirty-six patients with angina pectoris or coronary insufficiency, many showing ischemic

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* Serum glutamic oxalacetic transaminase activity and liver injury will be the subject of another communication.

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**Fig. 7.** Divides the serum glutamic oxalacetic transaminase curves following myocardial infarction in three groups: the connected squares represent the mean values, the circles the highest group of values and the triangles the lowest.

T-wave inversion or other equivocal electrocardiographic changes, have been studied and will be reported later in detail. Twenty-one had normal serum glutamic oxalacetic transaminase levels which fitted well with the classical picture. Fifteen with nonspecific electrocardiographic changes had elevated enzymatic activity of their serum, and therefore, presumptive evidence of heart muscle damage. Studies are in progress on serum glutamic oxalacetic transaminase in subendocardial infarction, following angina or coronary insufficiency associated with equivocal electrocardiographic changes, and in patients with acute rheumatic fever. When the enzymatic activity has been elevated in these patients, there has usually been some clinical evidence of active muscle damage.

Homogenized heart muscle of dogs contains approximately 400,000 units of serum glutamic oxalacetic per gram of homogenized tissue.7 If all the enzyme present were released into the blood of a 30 Kg. dog the level in 1 ml. of serum would be approximately 400 units. That this is the mechanism by which serum glutamic oxalacetic is elevated following myocardial infarction is suggested by the fact that samples of infarcted heart muscle may contain as little as 4000 units per gram. Further evidence that the enzyme is released from damaged cells is
provided by the fact that serum glutamic oxalacetic transaminase rises precipitously and in proportion to the time elapsed after death of the mammal studied.3

Figure 8 shows the precipitous rise in serum glutamic oxalacetic transaminase following death. Of note is not only the magnitude of the elevation but the fact that samples from the jugular vein remain consistently low (40 units) when samples drawn from the superior vena cava at the same time may contain as much as 280,000 units. Since the enzyme is high in brain tissue there must be a blood brain barrier preventing the escape of serum glutamic oxalacetic transaminase from brain tissue into the circulation.

It is important to emphasize that infection, stress of various kinds, and metabolic, neoplastic, degenerative or congenital diseases do not alter the serum glutamic oxalacetic transaminase unless actual damage of tissue occurs. Thus, in neuromuscular, respiratory, cardiovascular, renal and skin diseases or blood dyscrasias in which active destruction of tissue can be excluded the serum glutamic oxalacetic transaminase is within normal limits. However, as in hepatitis, in some patients with rheumatic myocarditis, dermatomyositis and acute myocardial or renal infarction, the level of serum glutamic oxalacetic transaminase rises in proportion to, and as long as, acute tissue injury is going on.

The level of serum glutamic oxalacetic transaminase appears to rise concomitantly with acute damage of heart muscle or liver cells and would appear to be a useful tool in detecting not only the presence of active cellular injury of heart muscle but also, in a rough way, the degree of damage. Its usefulness in detecting muscle damage associated with angina pectoris, coronary insufficiency, rheumatic and other types of myocarditis holds promise but cannot be evaluated without further study.

The method of analysis is relatively simple, requiring only five minutes per determination. The results are reproducible in the same and different laboratories and the enzyme is stable for several days when stored at 0 to 5°C.

Conclusions

Serum glutamic oxalacetic transaminase was present in all human sera tested.

The normal range of activity at 20°C is 8 to 40 units with a mean of 20 units.

Experimental myocardial infarction is followed consistently by a serum glutamic oxalacetic transaminase elevation of 2 to 20 times normal within 48 hours.

In 49 of 50 patients with transmural myocardial infarction serum glutamic oxalacetic transaminase activity rose 2 to 20 times normal during the first three days.

There appears to be a rough correlation between height of the serum glutamic oxalacetic transaminase activity and the size of the myocardial infarct.

Elevation of serum glutamic oxalacetic transaminase has been noted in conditions in which active destruction of heart muscle, skeletal muscle or liver occurs.

Serum glutamic oxalacetic transaminase is unaffected by angina pectoris, coronary insufficiency, heart failure, or digitalis in the absence of active heart cell damage.

Although serum glutamic oxalacetic transaminase appears to be an index of heart muscle destruction, its role in the diagnosis and management of heart disease will require further clinical study.

![Fig. 8. Describes the serum glutamic oxalacetic transaminase activity of blood withdrawn four to 36 hours after death of a normal dog. Note the differences in enzymatic activity when blood was withdrawn from the inferior vena cava, the right ventricle, the thoracic pool and that secured from the external jugular vein.](image-url)
Conclusiones in Interlingua

Transaminase oxalacetic glutamic esseva presente in omne specimens de sero human examine.

Le activitate normal a 20 C. varia inter 8 e 40 unitates con un valor median de 20 unitates.

Infarcimento myocardiac experimental es invariabilemente sequite intra 40 horas per un elevation del transaminase oxalacetic glutamic del sero a inter 2 e 20 vices le norma.

In 49 ex 50 patientes con infarcimento myocardiac transmural le activitate del transaminase oxalacetic glutamic del sero se augmentava durante le prime tres dies a inter 2 e 20 vices le norma.

Il pare existir un grossier correlation inter le magnitude del activitate de transaminase oxalacetic glutamic del sero e le dimension del infarcimento myocardiac.

Un elevation del activitate del transaminase oxalacetic glutamic del sero esseva observate in conditiones in que il occurre un destruction active del musculo cardiac, del musculos skeletal, e del hepate.

Le transaminase oxalacetic glutamic del sero non es afficite, in le absentia de active lesiones de cellulas cardiac, per angina de pectore, insufficientia coronari, dysfunctionamento cardiac, o digitalis.

Ben que le transaminase oxalacetic glutamic del sero pare esser un indice del destruction del musculo cardiac, su rolo in le diagnose e le tractamento de cardiopathia require studios clinic additional.

Acknowledgment

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